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Sobotta - Piersol

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SOBOTTA-PIERSOL
HUMAN HISTOLOGY

TEXTBOOK AND ATLAS OF
HUMAN HISTOLOGY
AND MICROSCOPIC ANATOMY

BY DR. JOHANNES SOBOTTA
PROFESSOR OF ANATOMY AND DIRECTOR OF THE ANATOMICAL INSTITUTE IN BONN

TRANSLATED BY
WILLIAM HUNTER PIERSOL
PROFESSOR OF HISTOLOGY AND EMBRYOLOGY IN THE UNIVERSITY OF TORONTO

VOLUME I: TEXTBOOK
WITH 42 DIAGRAMMATIC ILLUSTRATIONS

VOLUME II: ATLAS
WITH 535 ILLUSTRATIONS ON 68 COLORED AND 24 UNCOLORED PLATES

1930

G. E. STECHERT & CO., NEW YORK

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HUMAN HISTOLOGY
AND MICROSCOPIC ANATOMY

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FROM THE FOURTH GERMAN EDITION, GREATLY ENLARGED AND ENTIRELY REWRITTEN

*WITH 42 DIAGRAMMATIC ILLUSTRATIONS
FROM ORIGINAL DRAWINGS BY W. FREYTAG*

1930

G. E. STECHERT & CO., NEW YORK

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Preface to the Fourth Edition

While the third edition, which was completely exhausted in a few weeks, was only an urgent, post-war edition, prepared with plates repurchased from abroad, and showed no alterations from the second edition, the present, fourth edition is almost a new book. A certain number of the plates reproduced by the newer process (see preface to second edition) have been taken over from the earlier editions. The employment of the costly, and in many regards unreliable process of lithographic reproduction, had to be abandoned. Consequently all the plates, the number of which has increased to ninety-two, have been produced by the same method.

For this, it was necessary to redraw the figures which previously were lithographed. Advantage was taken of this opportunity to render under greater magnification a large number of the figures from the first, small, pocket-size edition. Moreover, the number of figures has been greatly increased and many figures of the older editions replaced by new ones. Since the preparation of the matter necessarily remained in the same hands as before and since the number of new figures was extremely large, the publication of the present book has been very greatly delayed. No small part of this delay was due to the fact that the artist could not carry on his work in the author's city, but except for occasional short periods here in Bonn, was compelled to pursue his work in Würzburg.

In contrast to the earlier editions it has proved necessary to separate Atlas and Text. The Atlas now embraces only the really typical, original contribution of the book as a whole; viz. the figures of preparations of (predominantly human) histology and microscopic anatomy. These now occupy ninety-two plates which for the most part are in color and are accompanied by explanatory text. Undoubtedly this part of the book may profitably be used by itself, *e. g.* in courses in microscopy. The other part of the book, the Textbook, contains a continuous presentation of histology and microscopic anatomy which is kept within the bounds of a textbook and which consequently, as in earlier editions, forgoes citations of the literature. As illustrations, the text is accompanied by thirty-seven diagrammatic figures. The simultaneous use of Atlas and Textbook is made easy by the marginal references in the latter to appropriate figures of the Atlas. In conclusion there is appended a brief account of the microscope and its use. Brief directions for making microscopic preparations are also given, but in view of the great number of methods an exhaustive presentation would be impossible within the bounds of the present book. For details the special manuals on this subject must be consulted.

I greatly regret that the present book has been so long delayed in appearing. The continuous enquiries concerning the book both from at home and abroad and the really unheard-of prices paid for the last copies of the book which remained on sale, have convinced me that my previous methods were correct. I hope that the book in its present form may enjoy the same favour as the earlier editions. For reading the proofs, I am under obligation to Dr. Quast, II. Prosector of the Anatomical Institute at Bonn.

The Author.

Bonn, April 1929.

73020

From the Preface to the First Edition

It was the original intention of the author to produce merely a histological POCKET-ATLAS with lithographic plates and to restrict the text to a detailed description of the plates. However it proved necessary to add a continuous descriptive text in brief form. The original drawings for the illustrations were prepared by *W. Freytag*, university artist, with the greatest care and exactness in a manner that makes them models. To facilitate the preparation of the original drawings a method was employed by the author of the book which involved *photographing* the preparations under the magnification at which they were to be drawn. The photographs then served as a basis for the drawings, an exact tracing of the outlines being transferred to the drawing-board.

This method guarantees not only an exact drawing of the outline and finest details but also a very exact enlargement, since measurements with a photographic camera are far more exact than those made with a microscope. Above all, sources of error in the drawing apparatus are eliminated, in particular the errors which become noticeable through the marginal enlargement which occurs in large fields under low magnification. As may be understood the photomicrographic positive affords a more exact reproduction than is possible to a pencil used with a drawing apparatus.

But the employment of photomicrographs has another great advantage. The positive picture after the tracing is made serves as a control during the preparation of the drawing. Since the details of a drawing, particularly of a general view, are almost always filled in with stronger lenses, there is great danger that the nuclei of the cells will be represented as larger than they should be under the magnification employed.

As regards the choice of preparations reproduced in the Atlas the principle has been followed, as far as possible, of picturing only *human* preparations and of using those from animals only where absolutely necessary, or where serviceable human preparations were not at the disposal of the author.

As a consequence of the above the Atlas has great value, not only for students as a guide in a course in microscopy, but also for the *practising physician* to whom even the best figures from animal preparations have only a limited appeal.

The figures of the preparations in this book have been made, almost without exception, at the magnifications obtainable with the ordinary systems of dry lenses used by students in courses in microscopy. Immersion lenses have been intentionally avoided except in delineating the finer details of a few of the figures. The minute structure of the protoplasm etc. of cells has not been exhaustively discussed for the same reason, since, in general, *figures and text of the Atlas, for students and physician alike, should contain all the essentials but should not go beyond this point.* Both in scope of material and in emphasis strict regard has been paid to the customary type of course in histology.

The arrangement of plates and text is such that, as far as possible, the former are found accompanying the text to which they belong. There are over eighty colored lithographic plates, while thirty-two of the sixty-eight figures in black have been printed as plates. In the few cases in which the distribution of space made a marked separation of text and figure unavoidable, notice is given in the text of the figure which corresponds.

Moreover the text is written as a continuous whole without special reference to the adjacent figures. The latter on the other hand, particularly the lithographed plates, are accompanied by special explanatory notes so arranged that the explanation is at the left, while the plate lies on the right.

Plate and text are consequently independent to a certain extent. The reader can read the text alone, or may study the plates through the explanatory notes independently of the text.

WÜRZBURG, November 1901. **J. Sobotta.**

From the Preface to the Second Edition

The relatively long time that has elapsed since the appearance of the first edition of this book is the chief reason for the radical alteration which the work has undergone in bringing it to its present form.

The format of the book has altered and in this regard conforms closely to the volumes of the Author's "Atlas of Descriptive Anatomy" from the same Press. The content of the book has been changed even more. Figures and text have both been so selected that they directly supplement the above named Atlas, or the Author's "Outlines of Descriptive Human Anatomy". At the same time the text of the first edition has grown from the compass of the small "Outline" to that of a short textbook. For in order that the book may not be unwieldy a manner of description must be selected which as far as possible shall be brief, and yet sufficient for both students and practitioners. For the same reason unimportant facts etc. have been to a great extent inserted as footnotes or in small type. For the first survey of the subject under consideration the student may pass over these additions without destroying the continuity of the presentation.

Of the fifty-six plates of the Atlas eight are in black and white, some as photogravures, others as zinc etchings (line and stipple). Thirty-two plates contain lithographs in several colors, many of the figures being those of the first edition; but there are numerous new figures. The remaining sixteen plates are polychrome prints made according to a process which I have described in detail elsewhere.[1]

The original drawings for the figures in the book again come from the extremely gifted hand of the university artist, *W. Freytag*, to whom I express my thanks for the great pains he has taken in the production of the book. Photomicrography has served as a basis for almost all the figures, the great value of which process for the higher magnifications, I have learned to prize more and more. Above all, this method guarantees the accuracy of the magnification given.

WÜRZBURG, 1911. **J. Sobotta.**

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[1] Zeitschrift f. wissenschaftl. Mikroskopie u. mikr. Technik, Bd. XXVII.

Translator's Preface

In preparing this edition in English of Professor Sobotta's "Textbook and Atlas of Human Histology" the intention throughout has been to translate, not to edit; to give not only the substance of the original but largely to retain its flavor as well. Although Vol. I, the Textbook, is primarily a sound exposition of the recognized facts of Histology, brief mention is also made of the more important unsolved problems. In a few of the latter cases the translator has added a comment of his own in the form of a footnote. In the matter of illustration of textbooks of histology the Plates of Vol. II, the Atlas, occupy a place which is both foremost and unique. The value of the Plates is evident at a glance and is attested by the manner in which a few of the figures have been used by other authors of textbooks of histology to give an added distinction to their volumes. The marginal references of the Textbook assure that the wealth of the Atlas shall be used to best advantage. It is from desire that this wealth should be available in the English language that the translation has been undertaken.

Toronto, July 1930. **W. H. Piersol.**

Contents

page

A. Histology, The Cell and the Tissues . . . . 1—130

I. The Cell, cellula . . . . 1—32

The Cytoplasm . . . . 3—9

The Nucleus . . . . 9—12

The Centrosome . . . . 12—14

Occasional Constituents, Cell Membranes 14

Syncytia (Plasmodia) . . . . 14—15

Pigment . . . . 15—17

The Phenomena of the Life of Cells . . . . 18—29

1. Amoeboid Movement . . . . 18—19

2. Reproduction (Cell Division) . . . . 19—29

The Duration of the Life of Cells and Their Death . . . . . 29—30

The Connections between Cells . . . . 30—31

Non-cellular, Secondary Constituents of the Human Body . . . 31—32

II. The Tissues, Histology Proper . . . . 32—130

Epithelial Tissue . . . . 32—52

Special Differentiations of Epithelial Cells . . . . 39—42

Secretion in Epithelial Cells . . . . 42—46

Glands . . . . 47—52

Endocrine Glands . . . . 47—48

Exocrine Glands . . . . 48—52

Supporting or Connective Tissue . . . . 52—96

1. Connective Tissue (Proper) . . . . 53—67

Gelatinous Connective Tissue . . . . 62—63

Unformed (Loose) Connective Tissue . . . . 63—67

a. Ordinary Loose Interstitial Connective Tissue . . . . . . 63—64

b. The Connective Tissue of the Serous Membranes 64

c. Areolar Connective Tissue . . . . 64—65

d. The Connective Tissue of the Inner Meninges 65

Formed (Dense) Connective Tissue . . . . 65—67

1a. Elastic Tissue 68

1b. Adipose Tissue . . . . 68—72

1c. Reticular (Connective) Tissue 72

page
2. *Cartilage* . . . 72—78
Hyaline Cartilage . . . 73—76
Elastic Cartilage . . . 77
Fibro-cartilage . . . 77—78
3. *Bone* . . . 78—82
APPENDIX I: The Cellular Elements of the Blood . . . 82—93
The Red Blood Corpuscles (Erythrocytes) . . . 82—86
The Colorless Blood Cells . . . 86—90
Blood Platelets . . . 90—91
Blood Dust, Haemoconia . . . 91
Appendix: The Cells of the Red Bone Marrow . . . 91—93
APPENDIX II: Endothelium . . . 93—96
Muscular Tissue . . . 96—110
1. Smooth Muscle . . . 96—99
2. Striated Muscle . . . 99—107
3. Cardiac Muscle . . . 107—110
Nervous Tissue . . . 110—130
1. *Nerve Cells (Ganglion Cells)* . . . 111—122
General Structure of Nerve Cells . . . 115—116
Special Features of the Various Types of Nerve Cells 116—121
Additional Cellular Formations of the Nervous System 121
The Connections of Neurones with One Another, the Neuropil . . . 121—122
2. *Nerve Fibers* . . . 122—128
Medullated Nerve Fibers . . . 123—127
Non-medullated Nerve Fibers . . . 127—128
3. *The Supporting Substance of Nervous Tissue, Neuroglia* . . 128—130

B. Microscopic Anatomy of the Organs . . . 131—310
I. Organs of the Skeletal System . . . 131—141
Bone . . . 131—134
Bone Marrow . . . 134—135
Appendix: The Development of Bones . . . 135—140
1. Endochondral Ossification . . . 136—137
2. Perichondral Ossification . . . 137—138
The Development of Bone in Skeletal Elements Which Are Not Preformed in Cartilage . . . 138—139
Post-embryonic Phenomena of Ossification . . . 139—140
Joints and the Connections of Bones . . . 140—141

page
II. Organs of the Blood Vascular System and of the Lymphatic System 141—158
IIa. The Blood Vascular System 141—148
1. The Heart, cor 142—143
2. *The Blood Vessels Proper* 143—148
a. The Arteries, arteriae 143—145
b. The Veins, venae 145—147
c. The Capillaries, vasa capillaria 147—148
IIb. The Lymphatic System 148—158
1. The Lymphatic Vessels 148—149
2. The Lymph Glands, lymphoglandulae 149—151
3. The Lymph Nodules, noduli lymphatici 151
4. The Spleen, lien 151—156
5. The Thymus, glandula thymus 156—158
III. Organs of the Muscular System 158—601
IV. Organs of the Nervous System 160—182
1. The Central Nervous System 160—174
a. The Spinal Cord, medulla spinalis 160—163
b. The Cerebral Cortex 163—168
c. The Cerebellar Cortex 168—171
d. Hypophysis and Pineal Body 171—172
e. The Membranes and Blood Vessels of the Central Nervous System 172—174
2. The Peripheral Nervous System 174—182
a. The Peripheral Nerves 175
b. The Peripheral Ganglia 175—177
α. The Cerebrospinal Ganglia 176
β. The Sympathetic Ganglia 176—177
c. Peripheral Nerve Terminations 177—182
α. Motor Nerve-endings 177—178
β. Sensory Nerve-endings 178—182
Muscle and Tendon Spindles 179
The Terminal Corpuscles 179—182
1. Tactile Cells and Tactile Corpuscles 180—181
2. End Bulbs (Lamellar Corpuscles) 181—182
V. The Organs of Digestion 182—221
1. The Oral Cavity 183—203
a. The Lips and Cheeks 183—184
b. The Teeth 184—187
Appendix: The Development of the Teeth 187—193
c. The Glands of the Oral Cavity (Salivary Glands) 193—200
General 193—195
The System of Excretory Ducts 195—196

page
Special Features of the Salivary Glands . . . . 196—200
The Serous Glands of the Oral Cavity . . . . 196—197
The Purely Mucous Glands of the Oral Cavity 197
The Mixed Glands of the Oral Cavity . . . . 197—200
d. The Tongue, lingua . . . . 200—203
The Papillae of the Tongue, papillae linguae . . . . . . 201—203
2. Palate, Palatine Tonsil, Pharynx . . . . 203—205
3. The Oesophagus, oesophagus . . . . 205—206
4. The Stomach, ventriculus . . . . 206—208
5. The Small Intestine, intestinum tenue . . . . 209—210
6. The Large Intestine, intestinum crassum and the Rectum, rectum . . . . 210—211
7. The Lymphatic Structures of the Intestine 211
8. The Blood and Lymphatic Vessels, and Nerves of the Stomach and Intestine 212
9. The Liver, hepar . . . . 212—217
The Gall Bladder, vesica fellea . . . . 217—218
10. The Pancreas, pancreas . . . . 218—219
11. The Peritoneum, peritonaeum . . . . 220—221
VI. The Organs of Respiration . . . . 221—229
1. The Nasal Cavities . . . . 221—222
2. The Larynx, larynx . . . . 222—223
3. The Trachea, trachea, and the Bronchi, bronchi . . 223—224
4. The Lung, pulmo . . . . 224—227
5. The Pleura, pleura 228
Appendages of the Respiratory Tract . . . .
1. The Thyreoid Gland, glandula thyreoidea . . . . . . 228—229
2. Parathyreoid Glands, glandulae parathyreoideae 229
VII. The Urinary Organs . . . . 229—237
1. The Kidneys, renes . . . . 229—235
2. The Ducts of the Kidney . . . . 235—237
VIII. The Male Reproductive Organs . . . . 237—249
1. The Accessory Glands of the Male Reproductive Organs . . . . 237—238
2. The Testis, testis . . . . 238—241
The Semen, Sperma, and the formation of the Spermatozoa . 241—244
3. The Seminal Ducts . . . . 244—247
4. Penis and Male Urethra . . . . 247—249
IX. The Female Reproductive Organs . . . . 249—260
1. The Ovary, ovarium . . . . 249—254
2. The Ducts of the Female Reproductive Organs . . 254—258
3. The External Female Genitalia 258

page
Appendix 1: The Suprarenal Gland, glandula suprarenalis . . . 258—260
Appendix 2: The Carotid Gland, glomus caroticum 260
X. The Organ of Vision . . . . 261—283
The Eyeball, bulbus oculi . . . . 261—280
1. The External Coat, Sclerotic Coat, tunica fibrosa oculi 261—264
2. The Middle Coat, Chorioid Coat, tunica vasculosa oculi . . . . 264—267
3. The Internal Coat, tunica interna oculi . . . . . . 267—278
The Pigmentary Epithelium, stratum pigmenti . . . . . 268—269
The retina . . . . 269—278
a. Pars optica retinae . . . . 269—276
b. Pars caeca retinae . . . . 276—277
c. Optic Nerve and Optic Papilla . . . . 277—278
4. The Lens . . . . 278—279
5. The Vitreous and the Zonule of Zinn . . . . 279—280
Accessory Organs of the Eyeball . . . . 280—283
1. The Eyelids and the Conjunctiva . . . . 280—282
2. The Lacrimal Apparatus . . . . 282—283
XI. The Organ of Hearing . . . . 283—294
1. The Internal Ear . . . . 283—290
a. Sacculus, sacculus, Utriculus, utriculus, and Semicircular Canals, ductus semi-circulares . . . . 283—285
b. The Cochlea, cochlea . . . . 285—290
2. The Tympanic Membrane and the Middle Ear . . . 290—292
The Eustachian Tube, tuba auditiva . . . . 292—293
3. The External Ear, auris externa . . . . 293—294
XII. The Organ of Taste 294
XIII. The Organ of Smell 295
XIV. The Skin, integumentum commune . . . . 296—310
Appendages of the Skin . . . . 300—310
1. The Hairs . . . . 300—303
2. The Development and Regeneration of Hairs . . . . . . 303—305
3. The Nails, ungues 305
4. The Glands of the Skin . . . . 306—308
The Mammary Gland, mamma . . . . 309—310
Appendix: The Microscope and its Use . . . . 311—328
I. The Microscope . . . . 311—317
II. The Use of the Microscope . . . . 318—323
III. The Measurement and Drawing of Microscopic Objects 323—324
IV. The Photography of Microscopial Preparations . . 324—325
V. The Technique of Microscopial Preparations . . . . 325—328
Index . . . . 329—345

A. Histology.

The Science of the Cell and the Tissues.

I. The Cell, cellula

The cell, cellula,[1] is to be considered as the structural unit of the human body, and Pls. 1, 2
also of the bodies of all plants and animals. It represents the smallest part of the body that leads an independent life. The cell is thus the smallest conceivable living organism. Consequently living beings, whether plant or animal, must consist of at least one cell even if this shows a very primitive character, such as the non-nucleated condition of bacteria. Living beings consisting of less than one cell, of a mere fraction of a cell, do not exist.

Since man belongs among the multicellular animals, or Metazoa, the human body is composed of a vast number of cells estimated at several trillions. For some time during embryonic life the human organism, like that of other animals, consists only of cells. Later, in a more or less advanced stage of development, there appear, as SECONDARY to the cells, other important structural constituents (p. 31). Although non-cellular, these are derived from the cells. Consideration of these is deferred until after that of the cells themselves.

All the cells of the human body are descendants of one single cell, the fertilized egg-cell or zygote, and are produced by a process of progressive subdivision. For cells are not formed out of a non-cellular matrix; a cell can only come into existence through the division of another cell.[2] As a consequence of this the embryo can, at first, consist only of cells.

The forms of cells are extraordinarily varied, but among human and animal cells two fundamental forms may be distinguished; spherical, and columnar, the latter being a more or less regularly six-sided, prismatic form. The fertilized egg cell, the ancestor of all the cells of the human body, or of the body of any animal, is almost exactly spherical. Its daughter cells and those of the next few generations approximate the spherical form but are distinctly flattened where they are mutually in contact. These cells, the so-called blastomeres, form the germ layers by grouping themselves into lamellar masses. In this arrangement the lateral surfaces are flattened by contact of cell with cell, so that the spherical form is lost and the cells become six-sided prisms.

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[1] The name "cell" is quite inappropriate for the animal unit and is borrowed from Botany. In contrast to animal cells those of plants, at least of the tissues of the higher plants, possess a cellulose membrane surrounding the cell itself, so that there is a cell-like enclosed space filled with cell contents. Such a relation does not obtain in animal cells.

[2] This fact which now seems almost obvious was not recognized for a decade after the discovery of the animal cell by THEODORE SCHWANN in 1839. The first to give expression to this fact "omnis cellula e cellula" was R. VIRCHOW in 1858. This idea in time displaced the earlier conception that cells could be formed out of a non-cellular matrix.

All other forms of cells, even the many cells of the human organism which present the most bizarre shapes, can be referred to one of these two fundamental forms. Free-swimming cells retain the primitive spherical form but are relatively infrequent. Those which combine to form the embryonic germ layers become prismatic cells. From these in turn are derived the great majority of the other cell forms.

Free-swimming cells, *i. e.* cells which are not combined into fixed associations, comprise among others those of the blood, the cells of which are either spherical (or almost spherical), or are disc-shaped. The sex cells or gametes are typical examples of free-swimming cells and it is their fate in time to become separated from the parent body. The female sex cell, the so-called egg cell, is a typical example of a spherical cell; while the male cell, being a flagellate cell, has power of independent movement and as a result departs considerably from the spherical form.

The size of an animal cell, and in particular the size of the human cell, varies greatly. Since cells generally are very small, and with rare exceptions are only to be recognized with the aid of a microscope, the unit of measurement used for them is the μ, the one-thousandth part of a millimeter. The smallest cells of the human body measure only 4—5 μ, occasionally even less, 3 μ. The largest cells attain a size that almost renders them visible to the unaided eye, 100 μ and over, for instance many nerve cells and the human ovum. The ova of many animals are of quite enormous size because they contain great quantities of so-called yolk; *e. g.* the yolks of chicken or ostrich eggs, eggs of sharks. The average size of human cells lies between 10 and 30 μ. Determination of the size of a cell is rendered much more difficult if the cell is thin, or greatly elongated, or flattened; or has very irregular contours, running out into numerous processes that are continually branching and becoming finer. This holds true for all cells which depart considerably from the fundamental spherical or prismatic forms.

Every animal cell consists of three principal parts designated CELL ORGANS in contrast to constituents of the cell, inclusions etc., which are less essential. The three chief organs of the cell are: I. the protoplasm, or better cytoplasm, also known as the cytosome; 2. the nucleus; 3. the centrosome. Perhaps some other constituents of the cell should hold a similar rank and be termed cell organs, *e. g.* Golgi's reticular apparatus; however our information as to the finer structure of the cell is not yet complete. Of the three fundamental constituents of the cell which can be termed such with certainty, the nucleus is occasionally lacking. But always such cells previously contained nuclei and in their non-nucleated condition possess only a short term of life, *e. g.* the red blood corpuscles.[1] But while occasionally non-nucleated cells occur there are no free nuclei devoid of cytoplasm, or in other words there are no cells without cytoplasm. The nucleus always lies surrounded by cytoplasm even when it has a highly eccentric position, and the same holds true for the centrosome which never occurs free or entirely by itself. In general nucleus and cytoplasm belong inseparably together; the nucleus is even a constituent part of the cytoplasm, in the wider sense of the word.

Of the three chief constituents of the cell the cytoplasm usually, but not always, has by far the greatest bulk; the nucleus comes next in size while the centrosome is exceedingly small. There exists a definite proportion between the amount of cytoplasm and the size of the nucleus; this is expressed by the term nucleo-plasmatic relation (p. 9).

---

[1] Bacteria are low forms of plant life, unicellular plants, which apparently continue through life without nuclei.

If a cell contains cell inclusions such as fat, pigment, glycogen, yolk etc. they lie almost without exception in the cytoplasm, only in rarest cases in the nucleus, never in the centrosome. These are materials which, in contrast to the living substance of the protoplasm, represent dead, non-living inclusions. The term reserve materials is also appropriate, especially in plant cells, for such substances.

Plant cells, especially those of the tissues of the higher plants, as a rule possess an additional chief constituent, the cell membrane. In animal cells, on the contrary, this is usually entirely absent; or if membrane formation does occur among the latter it is almost without exception only partial, that is it develops over only a small part of the cell.

In resting cells the three cell organs, cytoplasm, nucleus and centrosome, are sharply separated from one another. This is particularly true of the nucleus whose boundaries may be most clearly seen, both in the living cell by reason of its high refractive index, and in the stained cell through its deep color. Nevertheless all three stand in an extremely close relationship which becomes specially manifest at the time of cell division.

The Cytoplasm

Examining closely the individual constituents it is evident that the **cytoplasm** has a constitution that must be described as almost fluid. In many plant cells it is actually a question of a truly fluid condition of the cytoplasm. Undoubtedly in animal cells the consistency of the cytoplasm is somewhat different from that in plant cells; it is in a condition which may be said to lie midway between fluid and solid. Animal (and human) cytoplasm has the consistency of quite soft jelly. Pl. 1 Pl. 2, Fig. 1

Cytoplasm has also been described as a disperse, colloidal system in which a purely aqueous phase is demonstrable; with a second phase of albuminoids containing water, and of lipoids, disseminated throughout it.

Cytoplasm owes its almost fluid consistency chiefly to its high content of water, 60—70% and over; in spite of which it can incorporate additional quantities since it swells in water, but not in physiological salt solution or in Ringer's solution. On the other hand it is not soluble in water. The chemical reaction of cytoplasm is weakly alkaline. In the fresh (*i. e.* living or surviving) condition cytoplasm frequently — but by no means always — appears perfectly transparent and structureless; but this is an insufficient basis for the conclusion that it is actually without structure. For while it is highly questionable whether all the structures seen in the plasma of the dead cell existed there before death, it is not possible to dismiss them entirely, especially since many of them are also visible in the living cell. Naturally it is not astonishing that there is no unanimity in the views on the structure of cytoplasm; the more so since in dead and fixed cytoplasm different structures will appear according to the method of treatment of the cells. The FILAR THEORY of the structure of cytoplasm as advocated by FLEMMING admits two different structural elements in cytoplasm; the one consists of fibers, the other is not fibrous and is perhaps to be considered as fluid and colloidal. The fibrils together constitute the FILAR MASS or MITOME, the non-fibrous elements the INTERFILAR MASS or PARAMITOME. Fig. 1

The mitome appears in the form of fibrils variously arranged, they may be long or short, and may pursue a wavy course. They possess a rather greater power of refracting light than does the paramitome. The fibrils may join with one another and thus form a more or less distinct network. The fibrils of the mitome, for the most part, are not homogeneous structures but contain within themselves extremely fine granules in regular Pl. 2, Fig. 1

arrangement, the so-called MICROSOMES or PLASMOSOMES.[1] On the contrary the paramitome appears to be without microscopic structure. Frequently the fibrils show a definite arrangement, such as running from the centrosome radially toward the surface of the cell, an appearance seen distinctly in many colorless blood cells and in the blastomeres of many eggs.

Other theories substitute in part an essentially different plan of cytoplasmic structure. According to them it possesses a FOAMLIKE or ALVEOLAR constitution and is thus sharply distinguished physically from true fluids, which are homogeneous. Even on the basis of a foamlike structure in cytoplasm it is still possible to imagine it a fluid in which the internal tension in the foam has produced a preference for a definite form. Such preference is lacking in homogeneous fluids and is a leading distinction between them and cytoplasm. It is clearly demonstrated in cells of rounded form which have been pressed flat and then released, for they will then return to their original form. Nevertheless, the conception of an alveolar structure in cytoplasm does not exclude the existence of fibrils, only it must be conceived that many of these fibrils, if not all, arise from the fusion of granules which lie in the alveolar walls; or they are simulated by the walls being elongated. Although so many experimental results support the view of an alveolar structure in cytoplasm, still the pictures obtained from fixed cytoplasm indicate a fibrillar network; it is impossible to conceive that the latter is altogether an artefact.

ALTMANN'S GRANULE-THEORY of the structure of cytoplasm gives first place to the numerous cytoplasmic granules which lie at or near the limit of visibility. It terms them BIOBLASTS and considers them, and not cells, to be the ultimate structural units of the body. From such bioblast granules all other structures of the plasma are supposed to be formed.

Taking the fibrillar network theory of cytoplasmic structure as a point of departure, Pl. 2, Figs. 5—7 the cytoplasm of the cell body consists, as a rule, not merely of mitome and paramitome but includes other constituents which have in part been already mentioned. Of these the **mitochondria,** also known as plastosomes and as chondriosomes, play the most prominent rôles in the cell, especially as regards many of its functions. These constituents of the cell may be very sharply and distinctly revealed by special methods of staining. Frequently they are demonstrable by reagents which stain fat, *e.g.* they are blackened by osmic acid, so that they must be considered to consist, at least in part, of lipoid material. They appear, as in the sex cells, partly in the form of fine, spherical granules of uniform size, partly, as in most adult and embryonic tissue cells, in the form of rods which are usually quite short, or of fibrils of more or less homogeneous appearance. But frequently such fibrils consist of a row of granules in contact with one another. Special names have been devised for the separate forms and recently in place of the general term mitochondria, formerly applied to all of them, the term PLASTOSOME or CHONDRIOSOME is used; while the term MITOCHONDRIA or PLASTOCHONDRIA is used only if the granules are simple and spherical. Fibrils when distinctly formed of rows of granules are named CHONDRIOMITOMES, but if they are smooth and appear on staining to be quite homogeneous they are named CHONDRIOCONTES or PLASTOCONTES.

These structures may be uniformly distributed throughout the whole space of the cell; or they may be concentrated into a small circumscribed zone, the whole mass being then termed the CHONDRIOME. Other names have been given to this body, in particular that of paranucleus has been used when it lies near the nucleus, as occurs at a certain stage in the maturation of the male sex cells. In the female sex cells the chondriome is usually present as the so-called egg-nucleus, in other cases the term pseudochromosome is used. Even if the significance of the plastomoses has perhaps not been made completely clear as yet, this much at least is certain, that they play an essential rôle in many of the processes of differentiation that occur within the cytoplasm.

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[1] Not to be confused with plastosomes, see below.

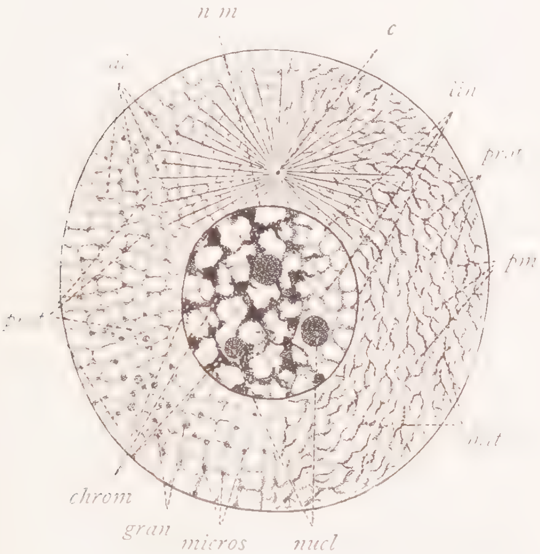

Fig. 1. **Diagram of the Structure of a Cell.** The right half shows the cytoplasm with fibrillar, the left half with alveolar or foamlike structure. In the nucleus only the network of linin is represented to the right, to the left the chromatin has been added.

al = alveoli
c = centrosome with radiation
chrom = chromatin
gran = granules
pm = paramitone
n m = nuclear membrane
lin = linin
micros = microsomes
mit = mitome and microsomes
nucl = nucleoli
prot = protoplasm

Consequently when important fibrillar structures appear in the cytoplasm as differentiation products it is probable that they have been derived through chondriocontes from plastosomes. These structures, then, are not part of the fibrillar substance of the cell, but are formed from the cytoplasm, and in particular from the plastosomes. They differ from the cytoplasm proper in the morphology of their finished state as well as in their physiological functions. Such are the myofibrils of the muscle cells, the neurofibrils of the nerve cells, most probably certain fibrils of the connective tissues, and the so-called tonofibrils of epithelial cells. Such fibrils lying in the cytoplasm have been characterized as paraplasm. There are also views which identify the plastosomes with Flemming's mitome and even with Altmann's granules. The granules that appear in the process of secretion are said to arise through the agency of plastosomes; and the basal filaments of many cells, such as those of the ducts of the salivary glands and of the convoluted tubules of the kidneys, may belong in the category of plastosomes.

Differing from the plastosomes, but included within the plasma, are other structures of granular form, the **chromidia.** They bear this name because they stain with the same dyes as does the chromatin of the nucleus; in fact the true chromidia arise from the nucleus and have migrated from it into the surrounding cytoplasm. In the higher animals, and particularly in vertebrates and in man, they do not at all play such a rôle as do the plastosomes; probably they occur in typical form only in the maturing egg-cells.

Perhaps the so-called **internal reticular apparatus** is to be classed with the above mentioned structures. It is a complex of structures which by no means always appear in the

Pl. 2, Fig. 8

same form, still less have they always received the same names. It was first observed and named as above in nerve cells, for in them it is exceedingly characteristic and well developed. At the same time the nature of the reticular apparatus is even yet not at all clear so that many would relate it to the plastosomes and others even to the chromidia. Certain forms of the reticular apparatus have been described as pseudochromosomes just as has been done for plastosomes; but probably reticular apparatus and plastosomes have nothing to do with each other. Where the reticular apparatus shows distinctly, as in nerve cells and in many gland cells, it gives the impression of a system of extremely fine anastomosing canals of somewhat variable caliber, whose order and arrangement in the different cells may be very different. In many nerve cells in which it is particularly well developed it is arranged about the nucleus in the form of a true perinuclear net; but in many other cells its extent is much more restricted. It is always located where the accumulation of cytoplasm is greatest; *e.g.* in columnar cells between the nucleus and the free surface of the cell; here, as usually elsewhere, it surrounds the centrosome. In doing so, particularly in cells which have but a small reticular apparatus, it usually lies close to the surface of the nucleus.

Since the reticular apparatus, besides being demonstrated by silver impregnation methods, is also blackened by osmic acid solutions, although much less rapidly than are fats, it may be considered as probably consisting of lipoid substances. However the results of many methods of fixing and staining show that beside the osmiophilic there is an osmiophobic substance in the reticular apparatus. It is unlikely that the lipoid substance lies in fine canal-like tubes in the cytoplasm; but it is probable that strands of such material anastomose more or less with one another, for the apparatus does not invariably consist of constituents which anastomose so distinctly as do those of many nerve cells. In the cells of many glands, and of other epithelia, in place of a true network there appears a greater or less number of curved fibers or rods which are indeed placed close together but show little or no anastomosis. Also there occur at times forms of reticular apparatus with very fine mesh, at other times the mesh is decidedly coarser; but it remains to be seen if these are not different functional conditions, for the apparatus appears to grow larger when the cell is larger, as in secretion. In this case it is observed that the first secretion granules appear in that region of the cytoplasm which shelters the reticular apparatus. Thus in gland cells there exists an intimate relation between the apparatus and the process of secretion, even if the details of the relation are not clearly understood.

In addition the reticular apparatus apparently takes an active part in the phenomena of cell division, for at the very beginning of the process it falls into halves which separate and enter the daughter cells. In the less compact form of the apparatus this is accomplished by a simple subdivision of its particles into two groups; in the more compact forms with true nets this subdivision is preceded by a breaking up of the network.

Although it is doubtful whether the reticular apparatus is present in plant cells, it has already been clearly demonstrated in most of the cells of vertebrates and of invertebrates, and in many of those of man; hence it may be assumed that it is a quite constant structure and an integral part of the cell, belonging to the cytoplasm from which it is not to be distinguished except as a specialized part. Apparently a reticular apparatus is absent only in short-lived cells destined to be destroyed, such as the red blood cells and cornified epithelial cells.

Another question, and one less easy to answer, is whether the internal reticular apparatus of the cell is identical with the so-called **trophospongium.** Under this name structures have been described which their discoverer, HOLMGREN, viewed as true intraplasmic canals and which he conceived to open on the surface of the cell. Even though the majority of the canals of the trophospongium might leave free the peripheral zone and occupy the perinuclear cytoplasm, yet it was a prime necessity that they should open on the surface of the cell; because their discoverer assumed that processes of other cells entered into these canals for the purpose of supplying nourishment. In the case of nerve cells these processes would come from the glia cells. However it appears that the trophospongium of nerve cells, and of some other cells in which it is just as sharply localized, is a structure equivalent to the internal reticular apparatus, and since this latter never presents an appearance corresponding to the external openings of the trophospongium canals the existence of such openings is at least doubtful.

On the other hand the so-called diffuse trophospongium described by Holmgren and demonstrated by him in cells of the liver, corpus luteum, deciduae and adrenal gland may belong to a quite different category; it has nothing to do with the internal reticular apparatus. In addition the same author describes in many other cells, such as young oöcytes and cells of columnar epithelium, a localized trophospongium which may, perhaps, be compared to the reticular apparatus of nerve cells.

The structure of cytoplasm set forth above is not always the same throughout its whole extent, frequently distinctions occur in different zones of the cell, especially as to the density of the cytoplasm; but this does not imply the existence of several kinds of cytoplasm within the one cell. Many cells are constantly observed in which the outer zone of cytoplasm differs from the inner zone, so that frequently an ectoplasm can be distinguished from an endoplasm. The latter is often the richer in inclusions of different kinds, one of which is always the above mentioned reticular apparatus. The ectoplasm rarely contains such admixtures but is rich in lipoids. Usually the one zone passes without demarcation into the other; but if the distinction between them is very great the ectoplasm constitutes a so-called CRUSTA which is not to be confused with the true cell membrane (p. 14 and Fig. 11), and is much more common than the latter in the cells of animals. Although such zones of ectoplasm rich in lipoids, have nothing to do with true cell membranes, under certain physical conditions they can replace the latter, as in red blood cells. The name ARCHIPLASM (archoplasm) has been given to still different portions of cytoplasm that form recognizable areas around the centrosomes, areas which under many methods of fixation are sharply delimited from the remaining cytoplasm. It has frequently been assumed that the centrosomes, the kinetic organs of the cell, concentrate around themselves the archiplasm as a constituent (kinoplasm) of the cytoplasm, which plays a rôle in the phenomena of movement in the cell. But it is probable that the differences between the archiplasm and the main mass of the cytoplasm are but differences in degree and without fundamental distinctions of structure. Amongst other things archiplasm lacks the cytoplasmic inclusions, granules, vacuoles etc., which occur in the rest of the cell; to a certain extent it stands in the same relation to cytoplasm as does ectoplasm. Pl. 1, Fig. 1

Of the more important structures found in the cytoplasm there are two classes which require special mention, the granules and the fibrils. As to the **granules** of the cytoplasm the mitochondria and the chromidia have already been considered; but there occur additional structures which are grouped under the term granules; although this general name covers structures of very different kinds.

The so-called ALTMANN'S GRANULES have already been briefly mentioned and it was explained that these structures, and still more the theories built upon their existence, have now only an historical interest. Pigment belongs among the granular structures of the cytoplasm but will be dealt with in a separate section. A wide range of cytoplasmic structures have been characterized as granules without it being exactly definable what should be understood by the term granule; certainly things of manifold origin have been described by this name. Neither is it certain that all the granular structures in the cell, for instance those which are demonstrable only by definite fixing and staining methods, were actually present in the cell during life. In addition granular formations may be of extremely different size.

Here belong, for example, the granules that can be demonstrated in the living or surviving cell by means of certain so-called intravitam stains. In what relation these structures stand to plastosomes, whether they are in a certain sense identical with them, or whether they are to be considered cytoplasmic inclusions of a paraplasmic nature, is as yet quite undecided. More nearly related to the plastosomes than to the granules just mentioned, but perhaps closely connected with the latter as well, are the so-called Arnold's granules to which have been ascribed important rôles in the metabolism of the cell.

The granular inclusions in the cytoplasm of the colorless blood cells appear to be similar structures. They vary in affinity for different kinds of dyes and have been divided into different groups on the basis of their peculiarities in this regard. Many of these
Pl. 11, Figs. 1, 15, granules are soluble in water. Still other inclusions of lipoid nature are found in cyto-
16, 20 plasm in the form of larger or smaller granules some, but not all, of which are combined with pigment (p. 15). Closely related to these are the yolk granules of the female sex cell, which when present in large numbers can give to the cell an enormous size.

Among the granular formations of the cytoplasm a most important rôle is played by the secretion granules; *i. e.* by the granular antecedents of the final secretion. Their existence stands in intimate connection with one of the most important processes in the life of the cell, that of segregation or secretion as it is to be observed in epithelial cells and particularly in the cells of glands. Such granules probably arise from the plastosomes of the cytoplasm through their agglomeration, in which state they probably undergo appropriate chemical changes, and at last after complete fusion the result is the mass of secretion granules. As granules they may be spherical or irregular in form, and being the antecedents of the fluid secretion they have been named zymogen granules. Since
Pl. 3, Figs. 10—12 they stain in an entirely different manner from the plastosomes, from which they have probably arisen, it may be assumed that a considerable change in chemical constitution was taking place while the secretion was maturing. The granules soon vanish, and the strong affinity for dyes which they possessed at first, is entirely lost as they become fluid. Granular structures such as these must be considered as paraplasmic constituents of the
Pl. 76, Fig. 4 cell; in their finished state they lie like foreign bodies in the cytoplasm from which they have arisen. Frequently the secretion is a lipoid, as in the sebaceous glands of the skin; in such case it is easy to see the distinction between the granules and the remaining cyto-
Pl. 92, Figs. 7—8 plasm. If reagents which dissolve fat are employed on cells filled with lipoid secretion granules, the cytoplasm takes on a pseudo-alveolar structure; in the place of the lipoid granules there appear pseudo-vacuoles.

In addition to granules there occur in the cytoplasm of very many cells **fibrillar** structures; but a sharp differentiation of the two types is not possible, as is shown by their relation to plastosomes which possess now a granular, now a threadlike form.

Yet there are in many cells cytoplasmic structures of quite pronounced threadlike or fibrillar character; to them belong in particular the myofibrils of muscle cells, the neurofibrils of nerve cells, the tonofibrils of epithelial cells, probably the gliafibrils of the neuroglia cells, and others. When fully formed they, like many of the granular structures, may probably be looked upon as definitely paraplasmic cell constituents. Although originally they were derived from the cytoplasm by differentiation, yet in their finished condition they differ from it distinctly, and often very widely. Further details of the true fibrillar structures will be given in describing the separate tissues.

The Nucleus

The second chief constituent of the cell — and one which in many respects is almost Pl. 1, Fig. 1
more important than the cytoplasm — is the **nucleus**. When the cell is at rest this is a sharply circumscribed structure which occupies a more or less central position in the cell. In many important respects the nucleus is to be distinguished from the surrounding cytoplasm; especially in the fixed and stained cell its appearance is much more distinct and evident than that of the cytoplasm. On the other hand in the living cell as Pl. 2, Fig. 1
a rule it is much less noticeable; it does indeed refract light more strongly than does cytoplasm but the difference in refractive index is not great. Nucleus and cytoplasm are, so to speak, opposites; as constituents of the cell they are extremely different, and the contrast between them runs all through both plant and animal kingdoms.

In most cells the nucleus is of less bulk than the cytoplasm, but neither in form nor in size does it vary so greatly as does the cytoplasm in this regard. The nucleus is greatly Pl. 14, Figs. 3, 4
inclined to take on a spherical form and relinquishes it only under compelling stress, as Pl 15, Figs. 1, 6
when the cell is greatly flattened or elongated. However there are cases in which, apparently without any special cause, the nuclear form becomes irregular so that spherical cells may have lobulated and polymorphic nuclei. On the other hand in cells of most bizarre form the nucleus is usually spherical. When the cell is at rest the boundary between nucleus and cytoplasm is very sharp, and in contrast to the cytoplasm this is marked on the part of the nucleus by a MEMBRANE. In many nuclei showing amoeboid processes it is said the nuclear membrane may be lacking. But important considerations are opposed to this assumption; perhaps in these cases the membrane is only very thin and the turgidity of the nucleus lessened. In spite of an undoubted structure in cytoplasm, it is still a disputed question whether the living nucleus possesses structure.

A cell almost always has but a single nucleus. Occasionally, but comparatively rarely, there are two.

While there is doubt as to the physical state of cytoplasm (p. 3), it is probably of the nature of a colloid; but there is no doubt that in the nucleus, constituents of firmer consistency can be distinguished from true fluids. By means of these the **nuclear membrane** is made tense and obtains its "turgor"; indeed the spherical form of the nucleus is essentially due to the nuclear sap. It has already been mentioned that the appearance of the nucleus in the living cell is not at all distinct, and the same is true of its most important part, the nuclear network. However if acetic acid is applied to a living cell both the nucleus and its network become distinct, since the acid makes the cytoplasm transparent without attacking the chromatic substance which forms the nuclear network. The latter stains easily with basic dyes — hence its name — so that although the nucleus contains achromatic constituents not stained by this method, it appears strongly stained by contrast with the cytoplasm. Because its reaction is alkaline cytoplasm naturally does not stain with basic dyes but, as a rule, does so at once with acid dyes. By employing at the same time a basic and an acid dye of different colors demonstration is made of nucleus and protoplasm by the contrast in staining.

If one examines the nuclei of living cells which have been treated with acetic acid, or of stained nuclei in a fixed preparation, the form of the nuclear network is seen to be highly variable. For the nucleus plays so prominent a rôle in the life of the cell that its appearance conforms to the activity of the moment. This is especially true of the nuclear network, which dominates the whole habitus of the nucleus. Especially in cell division the nucleus, and above all its network, plays a most important rôle and suffers radical changes in its structure. Consequently the nucleus of a cell during a prolonged rest appears quite different from that of a cell just formed by the division of a mother cell, or of one in the act of division. Indeed there is an essential difference in the appearance of those nuclei of a tissue which are chiefly involved in cell division, and of those nuclei which never divide. The same holds true for the other functions of the cell in which the nucleus plays a part *e. g.* secretion; and not only for the chromatic network of the nucleus but also for a secondary constituent, the nucleolus.

Every nucleus consists of two different substances which, according to their relation to basic dyes, are characterized as either the chromatic or the achromatic constituent. Of these the chromatic substance is the one which, biologically, plays the chief rôle in the nucleus; while the achromatic substance acts rather as a supporting material. Only the former can be called permanent nuclear substance since it alone exists longer than the stage lying between two cell divisions; while the achromatic material dissolves completely at each division, and each time is formed anew.

Fig. 1
Pl. 1, Fig. 1
Pl. 2, Fig. 1

The substance forming the achromatic network of the nucleus is given the name of **linin** or plastin; the nuclear membrane is probably formed of the same material. Its threads support the chromatic substance and are bathed by the nuclear sap. According to another view the achromatic substance of the nuclear membrane differs from linin and is termed AMPHIPYRENIN. Linin is not at all visible in the living cell, and even in the fixed and stained cell can be recognized only with difficulty, because as a rule the framework which it forms is quite concealed by the accompanying chromatin. It can best be seen when the cell and nucleus are preparing for division and the chromatin is concentrated into the so-called chromosomes (p. 21). It appears then as uniformly fine fibers which form a true network and pass without interruption into the equally achromatic nuclear membrane. It is entirely inactive toward stains and shows a marked resistance to acids and alkalis.

When the cell is at rest, the most important constituent of the nucleus, the chromatin, is distributed throughout this nuclear network. It may take on a coarse appearance as of stout bars and larger or smaller lumps; or at times it may be subdivided into extremely fine, dustlike particles. The knots of the linin network are favorite places for the deposition of chromatin, as is also the nuclear membrane itself. The latter may receive so much chromatin that a chromatic nuclear membrane may appear lining the achromatic membrane. The picture of the chromatic network formed by the chromatin situated on the linin network may vary to an extraordinary degree, not only in the nuclei of different cells, but also in different functional conditions of the same cell. Large droplets of chromatin which have accumulated at the knots of the linin network have given rise to the term PSEUDONUCLEOLI, because they may attain the size of the true nucleoli to be discussed further on.

The chromatin of the resting nucleus is thus more or less finely divided, and it may be asserted that the longer the resting stage lasts the finer does the subdivision of the chromatin tend to become. In such cases the chromatin network is not obvious, indeed even when stained it may be difficult to discover; at the same time, as a rule, the development of nucleoli is very distinct. On the other hand the nearer the time of cell division with its accompanying activity on the part of the nucleus, the more striking does the chromatin network become; so that in cells just previous to this process, and in young daughter cells, it is specially distinct. As a rule, in these cases nucleoli are absent. The differences in the distribution of the chromatin, together with the nucleoli, dominate the general picture, the habitus so to speak, of the nucleus.[1]

Pl. 1, Fig. 2

The chromatin of the nucleus derives its name from the fact that it is stained readily and intensely by basic dyes; since the albuminous substances, termed nucleoproteids, which form it contain free nucleic acid in varying amount. But not all the chromatin of the nucleus is BASICHROMATIN, along with it there occurs in varying quantity a kind which shows just the opposite reaction and on that account is termed OXYCHROMATIN. The proportionate amounts of the two kinds of chromatin varies with the functional condition of the cell, so that oxychromatin is entirely absent during the division of cell and nucleus. On the other hand, corresponding to the differences described above in the distribution of the chromatin, it would appear that in very inactive nuclei the oxychromatin increases at the expense of the basichromatin. Apart from the distribution of the chromatin and the behavior of the nucleoli, yet to be discussed, the whole habitus of the nucleus depends chiefly upon the proportions in which basichromatin and oxychromatin are present.

Minute investigation of the bars, droplets and strands of chromatin in the resting nucleus shows that they are not simple masses but consist of very fine granules, the so-called chromioles, which again can be distinguished as either basophile or oxyphile. In the coarser bars of chromatin the former, and in the finer bars the latter, predominate.

Another constituent of the nucleus, commonly but not invariably present, is the **nucleolus**. Occasionally it is the most striking part of the whole nucleus, especially so in living cells where it is often the only nuclear constituent visible. Such prominence is due to its high refractive index; to which may be added the fact that it is best developed precisely in those extremely inactive nuclei in which the chromatic network is very delicate and difficult to see. Frequently in such nuclei, even in stained preparations, only the nucleolus and the nuclear membrane are apparent and all the remaining nucleus seems filled with nuclear sap; since the oxychromatin, now so abundant, is recognizable only with difficulty. Typical examples are the nuclei of most nerve cells. This picture also shows very clearly in the oöcyte or egg cell taken from the Graafian follicle of the mammalian ovary and examined while fresh. The nucleus then appears like a vesicle (germinal vesicle of K. E. von BAER) filled with fluid, in which the large and highly refractive nucleolus (germinal spot) is alone visible.

Pl. 1, Figs. 1, 2
Pl. 16, Figs. 2—4
Fig. 7
Pl. 71, Figs. 1—

Usually the nucleus contains but one nucleolus, but there may be several; and occasionally, but never in man, very many. In the majority of cases its form is approximately spherical and when but one is present it almost always lies exactly in the middle of the nucleus. Usually it is a compact body but it may contain vacuoles. It consists, at least in most tissue cells but not in many female sex-cells, of oxychromatin. If an acid and a basic dye are used at the same time true nucleoli, (but not the pseudonucleoli mentioned above), will be stained by the former, and the basichromatin by the latter.

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[1] Concerning pycnosis of the nucleus see page 29.

Pl. 3, Fig. 8
Pl. 15, Figs. 2, 3
Pl. 16, Figs. 2, 6

As already stated, the presence of nucleoli indicates in general that the nucleus is in the resting condition. The nucleolus regularly disappears when a cell begins dividing; and new nucleoli do not form until some time after the complete separation of the daughter cells. It appears as though in this process the substance of the nucleolus dissolves; or according to another view is expelled from the nucleus previous to division. Frequently in many cells an extensive vacuolization of the nucleolus is observed to precede its dissolution.

It would appear that the nucleolus, in its growth, has intimate relations with the chromatin. The nucleus of a young daughter cell is very small immediately after division but it certainly grows considerably during the resting stage, at least until it attains the normal nuclear size for that tissue. It is quite conceivable that for this purpose the growing nucleus attracts the oxychromatin of the nucleolus that had dissolved in the cytoplasm, and so enlarges; for the amount of oxychromatin actually increases during the period of nuclear rest.

Whether nucleoli lie free within the nucleus, or are connected with the chromatic network, is not yet certain. In favor of the latter view it may be said that around the nucleolus (of oxychromatin) there is found a covering of basichromatin.

The oxychromatin of which the nucleolus consists is also termed paranuclein or pyrenin. This substance is comparatively resistent to reagents, especially to alkaline reagents.

The important rôle which the nucleus plays in the life of the cell is not confined to the phenomena of cell division yet to be discussed; but may be demonstrated, for example, by the distinct changes in nuclear structure which accompany the different phases of secretion in the cells of glands. Further, there occurs during various other phenomena of the life of the cell, an exchange of constituents between nucleus and cytoplasm which is doubtless mutual. However an exact demonstration of this exchange is often quite difficult to obtain, for the pictures seen under the microscope bear different interpretations. Yet beyond doubt the nucleus does send out substances into the cytoplasm; such have already been described (p. 5) under the name of chromidia. But the views differ greatly as to what structures of the cytoplasm come from the nucleus, and how far they are specifically formed within it. On this point some of the diverging statements have gone too far.

That the nucleus derives substances from the cytoplasm is also beyond all doubt. This is best seen in the fact that during mitosis all the achromatic constituents of the nucleus, including the nucleoli, disappear; they probably dissolve in the protoplasm and from it, later on, are again formed anew.

That nucleus proceeds only from nucleus is a fact long since proved; it may be confirmed in every detail, especially in the division of cell and nucleus. Over against Virchow's phrase ,,omnis cellula e cellula" may be placed as a complement the formula "OMNIS NUCLEUS E NUCLEO".

The Centrosome

Pl. 1, Fig. 1
Pl. 2, Fig. 1
Pl. 4, Fig. 5

The third, and by far the smallest, of the three chief organs of the cell is best known as the **centrosome**; although the term "central body" is sometimes applied to it. It is usually very small; nevertheless it plays an essential role in the cell, especially during cell division. Corresponding to its chief significance in the cell it may be considered as the KINETIC ORGAN of the latter.

The centrosome is often difficult to demonstrate in the resting cell; it appears very unobtrusive, and as a rule very small. Almost without exception it is located in the cytoplasm and only very rarely within the nucleus. It is most distinctly in evidence during cell division, and particularly so when one division follows closely upon another, as during the segmentation of the fertilized egg; then it is not merely distinctly recognizable but is often very much larger than in the resting cell.

Even in the resting cell the centrosome can usually be demonstrated with the aid of special staining methods. In most human tissues it appears in the form of a DIPLOSOME; *i.e.* of two small, rather spherical, granules lying closely side by side. In size these granules are usually less than one μ. Such a diplosome is usually surrounded by a small, but often ill-defined, area commonly known as the CENTROSPHERE. But the centrosome is not necessarily double in tissue cells, here as elsewhere it may be single; or under special conditions the number may be more than two.

Pl. 1, Fig. 1
Pl. 4, Fig 5

As mentioned the centrosome almost always lies in the cytoplasm, frequently near the nucleus, often indeed extremely close to it. But at times it may be widely removed, as in columnar cells, in which case it is found as a diplosome in a small clear area quite near the free surface of the cell.

It has already been pointed out that the protoplasm of this region surrounding the centrosome bears the special name of archiplasm; yet in certain cases, which are particularly numerous in human tissue cells, there this special differentiation of the protoplasm around the centrosome is lacking.

Pl. 1, Fig. 1

Like cytoplasm and nucleus the centrosome is a permanent organ of the cell, and like them it multiplies by division; so that a similar rule obtains as for the nucleus and for the cell as a whole: "OMNE CENTROSOMA E CENTROSOMATE".

In most human tissue cells the centrosome is small in size, usually not exceeding one μ and often less. The form, as a rule, is that of an irregular sphere but centrosomes do occur in short rodlike forms. In cells with several nuclei (polykaryocytes) and also in those with large, lobulated nuclei[1] (megakaryocytes) centrosomes are usually present in greatly increased numbers.

In ciliated cells the centrosome apparatus appears to be multiple, taking the form of the so-called basal corpuscles. These structures, in which the cilia of certain epithelial cells are rooted, are considered as derivatives of the centrosome. It must be assumed that during the transformation of the indifferent cell into a ciliated cell the centrosome became subdivided into a large number of single centrosome-like structures, the basal corpuscles. This idea has not yet been established by direct observation and is attacked from many sides, but is rendered plausible by the fact that in these highly motile cells the centrosome apparatus appears as the kinetic organ of the cell. Also in ciliated cells the centrosome does not appear in the form of a diplosome as is customary among non-ciliated epithelial cells. On the contrary the opposite view assumes a true diplosome in ciliated cells.

Pl. 3, Fig. 3
Pl. 4, Fig. 7

Occasionally in a cell which is resting, and not in process of division, there is seen proceeding from the centrosome a protoplasmic radiation like that which as a rule accompanies the centrosome at the time of cell division. The centrosome then forms the point from which the rays diverge. In the wandering cells (colorless blood cells) of amphibia this appearance is regularly observed. The great and peculiar significance of the centrosome finds expression in cell division (p. 19). In cells which after a short resting

Pl. 10, Fig. 4

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[1] Large lobulated nuclei are probably formed by the fusion of several single nuclei, fusion of the cells having previously occurred (see syncytium p. 14).

Pl. 2, Fig. 1 period quickly divide again there is seen during the brief resting stage a radiation in the protoplasm surrounding the centrosome.

In chemical composition centrosomes probably stand much nearer to the cytoplasm than to the nucleus. Toward stains their reaction is very similar to that of the former, for which reason under certain circumstances, especially in the resting condition of the cell, they are so difficult to demonstrate, surrounded as they are by cytoplasm.

Occasional Constituents of the Cell, Cell Membranes

In contrast to the three cell organs, cytoplasm, nucleus, and centrosome, which are constant in their occurrence, the cell membrane is very frequently absent in animal cells, and as a rule when present at all is but partly developed. This is also in contrast to plant cells, and particularly to the cells of the fully developed tissues of most plants.

In the cells of animals and in human cells a distinction must be made between a membrane which surrounds the entire cell and is termed the PELLICULA, and one which covers only a circumscribed portion of the cell and is known as the CUTICULA. The former are quite rare and of but slight thickness, and are in no way comparable to the cellulose membranes of plant cells. On the other hand in animal and human cells cuticulae are very frequent.

Perhaps the so-called sarcolemma of striated muscle fibers (p. 96) is, in part, to be considered as a pellicle, but not so the membrane of the cells of adipose tissue. A true membrane is simulated in female sex-cells by the so-called oölemma which is formed by the fusion of the cuticle of the egg cell with the cuticulae of the surrounding epithelial cells.

Pl. 2, Fig. 7 Partial membranes, cuticulae, occur under many forms and appearances on the free
Pl. 3, Fig. 2 surfaces of those cells which are associated to form an epithelium; they form one of the
Pl. 49, Fig. 4 most essential features of many varieties of epithelium.

Pellicle and cuticle are unlike exoplasm and crusta in being sharply separated from
Pl. 52, Fig. 1 the cytoplasm; from which they also differ fundamentally both in their behavior toward stains and in their physical properties such as refractive power. A gradual transition to cytoplasm is lacking in the formation of membranes and pseudomembranes but is the essential feature in the formation of a crusta.

Syncytia *(Plasmodia)*

In contrast to the individual cell which, with rare exceptions, has but ONE nucleus and ONE centrosome, there stand cellular structures which consist of a single mass of cytoplasm and several, or even many, nuclei; and a corresponding number of centrosomes. Such a structure is known as a SYNCYTIUM or PLASMODIUM.

The term syncytium is properly applied only to those multinucleate masses of protoplasm which have been formed by the fusion of cells that originally were separate; while plasmodia arise when centrosomes and nuclei divide, but the cytoplasm of the mother cell fails to do so. Both methods produce quite similar structures which, in the absence of proofs as to their origin, are usually termed SYNCYTIA.

A typical syncytium comprises a mass of cytoplasm, within which lie nuclei, commonly at very regular intervals. The amount of cytoplasm is usually considerable; the nuclei may number hundreds, even thousands, and for each there is a corresponding centrosome, usually close by. True syncytia of this kind, although frequent in lower animals and in the human body during its development, are rare in adult man. The striated muscle fiber is a typical example of a true syncytial formation.

Fundamentally there is no difference in kind between multinucleate cells (polykaryocytes) and syncytia; the difference is one of degree. Yet, as a rule, it is so marked that there can be no doubt as to what should be designated a multinucleate cell, and what a true syncytium. In multinucleate cells the nuclei draw together in a group, or even fuse and produce a megakaryocyte; and the centrosomes are similarly grouped in a more or less central position. In a true syncytium nuclei and centrosomes lie at quite regular distances from one another.

The term syncytium is used only when the general multinucleate mass of protoplasm is a single, complete structure. Cell networks formed by branching cells whose processes are joined and whose cytoplasm is continuous are not known by this name, although in principle they really are syncytia.

Pigment

All the colors which are found in the organs and tissues of animals and of man, ranging from the palest yellow to the most intense black are due to so-called PIGMENT. Pigment itself is one of the cellular inclusions found in protoplasm. Thus in the great majority of cases in which pigmentation appears, it depends upon pigment granules contained as inclusions in the cells of the tissue or tissues in question. The color of the tissue is determined by the color of the granules while the intensity of the coloration usually depends upon their number, rarely upon their size.

However it cannot be said that all pigmentation or coloration in the bodies of men and animals depends exclusively upon pigment granules; for there are diffuse pigments which give a decided color to tissues or fluids. The red coloring material of the blood is such a pigment in solution, but it is found in only one variety of cell. Another coloring material in solution is that of the bile, formed by modification of the pigment of the blood. But diffuse pigment in solution also occurs along with pigment granules; *e. g.* in the retina, both as the visual purple of the rods and as the yellow pigment of the macula lutea. The color of the hair is due partly to pigment as granules and partly to diffuse pigment.

In the vast majority of cases pigmentation is due to "granules" which are cell inclusions. Since the human body, especially that of the white races, is poor in pigment in contrast to that of most animals, pigment in great amount is found only in restricted regions such as the external skin, and more abundantly in the hair and eyeball. Apart from the latter organ, pigment is of relatively rare occurrence in the interior of the human body.

The pigment of the body is not everywhere of the same nature; considered chemically there are different kinds of pigment. Of these the most widely distributed, not only among highly pigmented animals but also in man, is the so-called **melanin pigment.** It does not always occur, as its name would imply, as a pure black; but is found as pigment granules of all shades. It is the pigment of the skin and of the eye, otherwise its occurrence is but rare and occasional. Two varieties of melanin pigment can be distinguished; melanin proper and the so-called FUSCIN pigment which occurs exclusively in the pigmentary epithelium of the retina.

Pl. 5, Fig. 6
Pl. 78, Fig. 4
Pl. 60, Fig. 3

Melanin in the narrower sense is by far the most common form of pigment, occurring most abundantly in the bodies of animals and also in the human body. It occurs as fine, approximately spherical granules which, as a rule, fill the entire cytosome. Their average diameter is 1 μ or less; in different animals the size varies but is constant in one and the same species. The color of a given tissue depends upon the color of the pigment granules; and its intensity upon how many cells contain pigment, and how closely they lie together. Melanin occurs in all the tissues except muscle, very sparingly in nervous tissue (cells of the substantia nigra), but abundantly in epithelial and connective tissues. The color of the skin in the colored races of man, and of pigmented areas in the skin of the white races, is due to its presence as an epithelial pigment in the epidermis. Melanin, as a connective tissue pigment plays an important rôle in many animals; and especially in the lower vertebrates there occur great numbers of large, branched, connective tissue cells filled with melanin granules. These cells are chiefly responsible for the pigmentation of the animals and for its ability to change. Pigmentation in human connective tissue is rare; so that melanin in the connective tissue layers of human skin is really exceptional, at least in the white races. Except under pathological conditions the chief seat of melanotic connective tissue in man is the connective tissue of the eyeball. Melanin is not soluble in either acids or alkalis, nor in reagents which dissolve fat; but only in concentrated nitric acid. Hydrogen peroxide "bleaches" melanin, and nascent chlorine is even more effective. Toward basic dyes and those which color fat it is quite negative; on the other hand it reduces silver nitrate.

Pl. 79. Figs. 3. 4 **Fuscin pigment** is a variety of ordinary melanin. As already mentioned it is present
Pl. 80, Figs. 1—7 in the pigmentary epithelium of the retina, and is distinguished both morphologically and chemically from ordinary melanin.[1] Here only the morphological differences from melanin will be considered. While the latter almost always occurs as fine granules of rather spherical form, fuscin appears in various forms, either as short, fine rods or needles, as in the pigmented layer of the retina, or as coarser, irregular particles such as are seen in the pigmented layer of the ciliary body and of the pars iridica retinae. Its color, as in the case of melanin proper, varies from light brown through darker shades to a brownish black.

Pl.16,Figs.2—4,7 **Lipofuscin pigment** differs essentially from melanin pigment in the widest sense of the words. As its name implies it is a pigment united with a lipoid. Reagents which dissolve fat also dissolve most of this compound, so that in preparations made with the aid of such reagents there often is no longer any pigment to be seen. The lipoid content of the lipofuscin granules is variable, either large or small; for fat-dissolving reagents may effect a complete solution of the pigment, or may fail to do so. It is much disputed whether the
Pl. 76. Fig. 3 lipofuscin is really united to a lipoid substance. Lipofuscin seldom appears in dark shades; it usually has a yellow or yellowish brown tint. Apart from its solubility in reagents which dissolve fat, it differs essentially from melanin in never filling the cytosome uniformly but being restricted to a quite circumscribed portion of the cytoplasm. Here the granules of lipofuscin accumulate; for, like melanin, lipofuscin appears in the form of "granules" or "droplets."

Lipofuscin is present in muscular tissue, especially in striated muscle fibers and those of the heart; also in many nerve cells and in the parenchyma cells of the epiphysis as the so-called pigment of wear and tear; but seldom in connective tissue. It agrees with melanin in being insoluble in acids and almost so in alkalis; further it is "bleached" by nascent chlorine, and less completely by hydrogen peroxide. On the other hand it is blackened by solutions of osmic acid, and is stained by Sudan and other fat-staining reagents. Unlike melanin it shows a distinct affinity for basic dyes.

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[1] It was given its name by von Kühne. In contrast to melanin it has been said, but not proved, to contain iron.

There is MORE CERTAINTY that **lipochrome** is a fat-containing pigment. It is similarly blackened by solutions of osmic acid and stained by dyes, which like Sudan, color fats. It is rare in the human body and really is found only in the so-called lutein cells of the corpus luteum. Like lipofuscin it occurs as granules and droplets which usually fill only part of the cytoplasm. In the retina it occurs as a solution in the area of the macula lutea to which it gives its color. Its behavior toward sulphuric acid is characteristic, for this reagent changes the color of lipochrome to blue or bluish green; but upon lipofuscin it has no effect. Lipochrome dissolves completely in solvents of fats.

These are known as autochthonous pigments because they are formed within the cell in which they lie, and from its constituents.

The question is not yet settled whether the pigment granules are formed from the cytoplasm or, as many facts seem to indicate, from the nucleus. It is often assumed that pigment granules, including those of melanin, do not lie free in the cytoplasm but are enclosed within bodies which carry the pigment, but are themselves unpigmented; so that when the pigment is removed by bleaching, the colorless pigment-bearers still remain. This would be similar to lipofuscin in which a lipoid material is the bearer of the pigment proper.

It is an open question whether melanin also occurs intercellularly. Although the histological picture does occasionally favor the possibility, as in the pigmented, branching figures in the bulbs of hairs, and in other epithelia; yet the occurrence of free, intercellular pigment is by no means proved. It is equally undecided whether pigment — and again melanin alone is in question — can be transported; that is whether it may be formed in one cell and then secondarily transferred to the cell in which it is found. Admitting this to be correct, although it is by no means proved, it is necessary to assume a special form of pigment-transporting cell which, like a wandering cell, becomes loaded with pigment and then at the end of its wandering hands over the pigment to another cell. To this hypothesis is linked a second: that pigment may be subjected to a process of phagocytosis and surrender as just described.

Pl. 90, Fig. 3

On the one hand it is asserted that connective-tissue cells can phagocytose pigment granules and so become pigment cells, and that they can appropriate pigment originally formed in epithelial cells of the epidermis. On the other hand the opposite assertion is made, that the deposition of pigment in epithelial cells can be effected by wandering connective tissue cells. These two assumptions show the uncertainty which surrounds this question.

The term "Dopa reaction" denotes the transformation of dioxyphenylalanin into melanin which consequently is considered to be the antecedent of melanin. This reaction, according as it is positive or negative, is supposed to indicate whether the pigment found in a cell was formed within that same cell, or whether it was transported to the cell in question by another. Opinions on the value of this reaction are very diverse.

In contrast to the autochthonous pigments stand the IRON-HOLDING PIGMENTS which are derived from haemoglobin, the pigment of the red blood corpuscles. They rarely occur except under pathological conditions; the only one normally observed, and that but seldom, is HAEMATOIDIN which may form in blood clots, and consequently is often found in the coagula in the center of corpora lutea (see Chap. IX). It occurs in crystalline form.

Among animals, especially the lower vertebrates (amphibia, fishes), are found the so-called melanophores, large pigment cells, more or less branched, and containing enormous quantities of melanin granules. A variety of these, the so-called allophores, contain a yellow or yellowish red pigment insoluble in alcohol. In addition there are the lipophores whose lipochrome pigment is yellow or reddish, and the guanophores containing the finely granular guanine pigment, frequently in crystalline form.

The Phenomena of the Life of Cells

In considering the phenomena of the life of cells there must be recalled the definition of a cell given previously (p. 1); that it is the smallest unit of the body that leads an indepedent life. But since a series of the processes are recognizable morphologically and must be studied with the aid of a microscope, their exposition falls within the range of histology. As may well be imagined physiology and morphology are here in very close touch.

In the cells of animals three different phenomena of the life of cells may be followed under the microscope: the movements of cells; the process of secretion; and reproduction.

Since the phenomena of secretion are connected exclusively with epithelial tissues they will be discussed along with the latter.

Of the three varieties of movement observed in the cells of animals[1] only one will be dealt with here, the so-called amœboid movement. Of the other two kinds, one, ciliary movement, is exclusively connected with epithelial tissue, and the other, muscular movement, with muscular tissue.

1. Amœboid Movement

Amœboid movement derives its name from one of the unicellular animals (protozoa) known as the amœba, in which locomotion is accomplished in exactly the same way as in the mobile cells of the bodies of men and animals. This type of movement is more widespread in the embryonic condition than in the fully developed organism, where it is rarely observed except in the colorless blood cells and in those most closely related to them. In this case the cell is spherical when at rest, and any part of its cytoplasm will serve for amœboid movement. In the performance of this movement the cytoplasm thrusts out processes, so-called pseudopodia, of variable size and number. They may extend outward or draw back, fuse together or draw apart, so that the cell is able to assume almost any form desired.

Pl. 2, Figs. 9—11

Amœboid movement progresses very slowly even when observed under strong magnification, which naturally appears to increase the rapidity of the movement. In the cells of cold-blooded animals observed under the microscope, noticeable changes in the form of a cell can only be recognized at intervals of 10—20 seconds.

If the dark-field condensor is used to observe amœboid movement, fine pseudopodia can be observed to precede the relatively coarse processes which alone can be seen with the clear field. The former processes seem to fuse with the latter.

The changes of form produced by amœboid movement serve a twofold purpose, locomotion and phagocytosis, both of them most important biological processes. Cells which change their locality through their power of amœboid movement are called wandering cells. Such cells can traverse almost all the tissues of the human body, and in doing so are not confined to pre-existing spaces but can penetrate the cement substance between epithelial cells and pass entirely through epithelia, even those of considerable thickness. They pass through the walls of the smallest blood vessels, the capillaries, by squeezing through the cement between the endothelial cells; for so the cells composing the wall are named. Countless millions of such cells are thus continually traversing the tissues of our bodies, naturally without the fact coming into our consciousness. There are but few tissues of the human body in which wandering cells are not found; in most places their occurrence can be counted upon with absolute certainty. For the production of amœboid movement, which otherwise is somewhat different from that of the amœba, oxygen is necessary; in its absence the movement ceases.

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[1] In the cells of plants an additional form of movement occurs, the circulation or rotation of the cytoplasm within the cell membrane.

Regarded biologically the phenomenon of **phagocytosis** is of the greatest importance. This term denotes the ability of amœboid cells to surround foreign substances by the action of their pseudopodia. These substances are thus rendered harmless and eventually digested. Such cells are known as phagocytes, which term, however, is also applied to certain fixed cells having phagocytic power. These also extend pseudopodial processes and thus are enabled to seize foreign bodies. Pl. 2, Fig. 10

The process of phagocytosis is of greatest importance for the body since much foreign matter of different kinds can be rendered harmless; *e. g.* bacteria, especially pathogenic bacteria; and inanimate foreign bodies, both organic and inorganic, such as dust from coal or other inorganic matter. The latter, in spite of the protection afforded by the ciliated epithelium of the air passages (p. 41), reach the alveoli of the lungs but are removed by phagocytosis (p. 226).

Most convincing evidence of the extent of phagocytosis, apart from the colorless blood cells, is afforded by injecting a considerable quantity of foreign matter into the subcutaneous lymph sac of a frog. Chinese ink, which consists of the finest possible particles of carbon suspended in fluid, is a suitable material. After 24—36 hours the lymph sac is completely free from it. The removal of the foreign material can only have been accomplished by the colorless blood cells, drawn there through the strong attraction which the foreign particles exerted upon them. That in fact a large proportion of the colorless blood cells of the frog have shared in the cleansing is easily shown by taking a drop of circulating blood from the heart; a large part of the colorless blood cells so obtained will appear laden with particles of ink. It must be admitted that colorless blood cells left the circulation at the lymph sac, and after phagocytosis of the foreign matter which had been injected, returned to the blood stream.

Amœboid movement is produced only by a stimulus; if none is present the colorless blood cells remain spherical and at rest. Naturally these free-moving cells are not under the control of the nervous system, much less under that of consciousness.

2. Reproduction (Cell Division)

The increase in number of the cells of the human body takes place exclusively by their division; the process is hence known as cell division. Another mode of increase is found in many lower animals in the form of so-called budding, but is not generally observed among the higher animals, nor in man. Increase has already been referred to in the pronouncement first given form by R. VIRCHOW: OMNIS CELLULA E CELLULA. Previously it had been generally assumed that cells could be formed from a non-cellular matrix, as are crystals from a salt solution.

It is generally accepted that there are two forms of cell division, which are distinguished by fundamental differences in the behavior of the nucleus in the two processes. The one is known as direct or amitotic, and the other as indirect, mitotic, or karyokinetic cell division. The significance of the latter is so overwhelmingly the greater that it must be looked upon as the normal manner by which the multiplication of cells is wont to proceed.

Direct or Amitotic Cell Division

As already stated this form of cell division plays quite a subordinate rôle. Although in this case the phrases omnis cellula e cellula, and omnis nucleus e nucleo, still hold good; yet the nuclei formed by this process are in no way to be considered equivalent to those formed by mitosis. If it cannot be denied that this represents the primitive mode of cell division, yet it is relatively very rare and mostly confined to ageing nuclei; and frequently goes only as far as nuclear division, the cytoplasm remaining undivided.

The process consists essentially of a simple, progressive constriction of the nucleus until what was a single nucleus becomes subdivided into two nuclei which usually, but not invariably, are of equal size. Then follows a simple constriction of the cytosome so that two uninuclear cells result; but if the constriction of the cytoplasm fails, a binucleate cell is formed. It is noteworthy that the centrosome in this process is relatively passive, a contrast to its behavior in the mitotic division of nucleus and cell.

During the process of its constriction the nucleus is seen to lengthen greatly, and then assume the form of a dumbbell, before dividing. Very frequently the subdivision of the nucleus is preceded by that of the nucleolus, which first becomes dumbbell-shaped and then divides. In the processes of the true growth of the body, especially during embryonic development, direct division of nucleus and cell does not in general occur; and even at other times it is seldom observed. Division of the nucleus in this manner appears to be more frequent than is complete division of the cell. Binucleate cells are formed in this way; examples are frequently seen in the liver, but usually only in comparatively young individuals. But elsewhere there occur binuclear and multinuclear cells, such as multinucleate giant cells or polykaryocytes, in which increase in the number of nuclei has proceeded in the direct mode, or has probably resulted from it. There are certain forms of cells in which it probably occurred and was subsequently followed by partial fusion of the nuclei; in such manner are formed large cells with great lobulated nuclei and several centrosomes. Such are the giant cells with large nuclei, the so-called megakaryocytes. However the mode of formation of such cells is not certainly known; it is even probable that the multiplication of nuclei in this case proceeds by mitosis (p. 93).

Indirect, Mitotic, or Karyokinetic Cell Division

Almost without exception, in the animal as well as in the plant kingdom, the multi-
Pl. 1, Figs. 3—20 plication of cells occurs by indirect cell division. The term karyokinetic is given because
of the peculiar movements of the nucleus and the changes in arrangement of its parts;
while the term mitotic refers to the threadlike structures which occur in the nuclear
region during the process.

As would appear from the terms applied, the nucleus of the cell exhibits the most
Pl. 2, Figs. 2—4 noticeable phenomena of this process, which also appear earlier than the division of
the cytoplasm. At the same time, or even earlier, the centrosome becomes active. The
three laws already formulated: omnis cellula e cellula, omnis nucleus e nucleo, omnis
Fig. 2 centrosoma e centrosomate here receive a precise confirmation.

Although as just mentioned the centrosome is wont to initiate the whole process, this description will begin with the changes on the part of the nucleus. Before the beginning of **mitosis,** as the process is commonly called for the sake of brevity, the nucleus usually enlarges somewhat and, what is of more significance, it loses its nucleolus if in the resting state it had one. Generally the amount of oxychromatin diminishes and that of basichromatin increases (p. 11). In addition a decided concentration of the latter occurs so that threadlike structures are to be recognized in the nuclear network. Although at first the threads may be poorly formed they continually improve at the expense of the irregular masses of basichromatin which previously predominated. The disappearance of the nucleoli probably depends upon, and accompanies the conversion of oxychromatin back again into basichromatin. The microscope frequently shows the nucleoli becoming vacuolized, the vacuoles becoming larger and larger, and the basichromatin shell of the nucleolus (p. 11) growing thicker until the latter is incorporated into the mass of chromatin threads.

The threadlike chromatic structures become more and more distinct within the nucleus, where naturally they are attached to the linin network. At first their contours are irregular and show pointed or toothlike projections; but the number of these steadily diminishes and the threads gradually grow smoother.

These threadlike structures, consisting of pure basichromatin, are called **chromosomes.** At first they lack definite arrangement and often show considerable length, being closely interlaced in the nuclear area to form a tight coil, the SPIREME. Frequently the impression is given that a single long thread had been formed from the chromatic network of the nucleus and that subsequently it divided into segments. However it is doubtful if all the chromatin of the nucleus is actually formed into a single long thread; probably in some cases it is so, but in other cases several threads may be formed.

With the formation of the chromosomes from the chromatin of the nucleus the process of mitosis proper is begun; the first few steps of it are grouped under the term the **prophase.** After the stage of the close spireme there follows that of the loose spireme or MONOSPIREME. The chromatin threads or chromosomes now become more clear-cut, usually they are rather shorter and thicker than in the stage of the close spireme, moreover their arrangement is no longer irregular as formerly was the case. Each chromosome has become bent, but not sharply so, into an angular, V-shaped thread, and all the chromosomes are oriented so that the bend in each is turned toward the same pole of the nucleus. The free ends of the loop — for so the bent thread is now called — are turned toward the opposite nuclear pole. In other words the chromosomes of the open spireme show a POLAR arrangement. The centrosome, or a structure which has been derived from it, lies at that pole of the nucleus toward which the bends of the loops are turned. Pl. 1, Fig. 8

In this stage of the open spireme, the achromatic constituents of the nucleus, the linin network and the nuclear membrane, dissolve; so that the chromosomes of the open spireme lie free and more or less centrally placed in the cytoplasm. The polar arrangement being regulated from the centrosome naturally remains unaffected. It is a characteristic feature of the process of karyokinesis or mitosis that the previously sharp boundary between nucleus and cytoplasm disappears. A cell caught in mitotic division is at once recognized by its lack of the self-contained nucleus of the resting stage; in its place there is now found the mitotic-karyokinetic figure. In the stage of the spireme the chromosomes are prominent in the microscopic picture, but in later stages there appear as well the achromatic elements of the karyokinetic figure. Thus from the moment of the dissolution of the nuclear membrane the chromosomes of the open spireme no longer lie, as in the resting stage, upon a linin framework, but free in the cytoplasm. Pl. 1, Fig. 8

The chromosomes which are formed from the nuclear network during mitosis are the most important structures in the process of the indirect division of nucleus and cell. As a rule, and this applies to human chromosomes, they have the form of a short cord. Having been formed from chromatic material they stain intensely with basic dyes; the latter may be aniline dyes or of plant or animal origin. The staining is more intense than that of the resting nucleus which indeed also contains achromatic elements. Chromosomes are not homogeneous in structure, they consist of most minute particles of chrom-

Fig. 2. **Diagram of Indirect Cell Division, Mitosis, or Karyokinesis.**

1. Cell with resting nucleus shortly before division.

The nucleoli have disappeared; the chromatin of the nuclear network begins to concentrate into chromosomes. Around the centrosome (diplosome) a radiation is developing.

2. Commencement of division; stage of the close spireme, prophase.

Within the nuclear membrane the chromosomes next appear in the form of an unbroken thread of chromatin, which has already begun to segment. The daughter centrosomes have moved apart, and between them the achromatic central spindle has developed.

3. Stage of the open spireme, prophase.

The nuclear membrane has dissolved and there no longer exists any boundary between nucleus and cytoplasm. Four chromosomes shaped like loops have formed and lie in polar arrangement with the bend directed toward the much enlarged spindle. Rays, later to be known as mantle fibers, proceed from the centrosomes to the chromosomes.

4. Monaster stage of mitosis; end of prophase.

The achromatic spindle has reached its fullest development and dominates the whole cell. At its equator the four chromosomes form the equatorial plate, monaster or mother aster; each chromosome shows a longitudinal cleft.

5. Commencement of metakinesis.

The daughter chromosomes have separated from one another and are drawing near the poles of the spindle; the process begins at the point where the chromosomes are bent. The cell is elongating.

6. Stage of the diaster, daughter asters, anaphase.

The daughter chromosomes form an aster near each of the poles of the spindle, which has now become barrel-shaped. The cell begins to be constricted opposite the middle of the spindle.

7. Diaster, more advanced.

The daughter asters have separated farther, and the constriction of the cell has increased.

8. Stage of the daughter spiremes, dispireme, anaphase.

The subdivision of the cytosome is complete. Nuclear membranes have formed around the chromosomes, now drawn together to form the two spiremes.

9. Telophase.

Division is now completed and resting daughter nuclei are formed, although the chromatin still shows recent activity by its arrangement; and as yet there are no nucleoli. The daughter centrosomes have divided and become diplosomes.

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atin, the so-called CHROMIOLES, tightly pressed together. Usually the chromioles are arranged in two parallel rows separated by a longitudinal furrow. The individual particles of each of the parallel rows are called CHROMOMERES; they are arranged one after another in the row and are closely connected. Probably the structure of the chromosome is even more complicated, it appears to possess an achromatic shell in which, in turn, further structure may be demonstrated.

The number of chromosomes entering into karyokinesis is always the same in all Pl. 1, Fig. 3 the cells of all the individuals of the same species. In vertebrates the number is usually 24 and according to the views of many this is true for man. However in the mitotic division of human cells the usual number of chromosomes to be observed is decidedly greater, and it is now established almost with certainty that the number is 48. In many animals it is much less; the least number being 4, found in the ascaris of the horse, and one variety of this ascaris has but two chromosomes. In some animals the chromosomes have different sizes or forms, but this does not appear to be the case in man.

Often as early as the stage of the open spireme there becomes visible in each chromo- Pl. 2, Figs. 3, 4 some a fine longitudinal cleft which at first had remained latent; but at times the cleft may not appear until toward the close of the prophase. It corresponds to the longitudinal furrow between the two rows of chromomeres. Along this cleft the chromosomes split from end to end, an action which is the most important step in the whole process of karyokinesis.

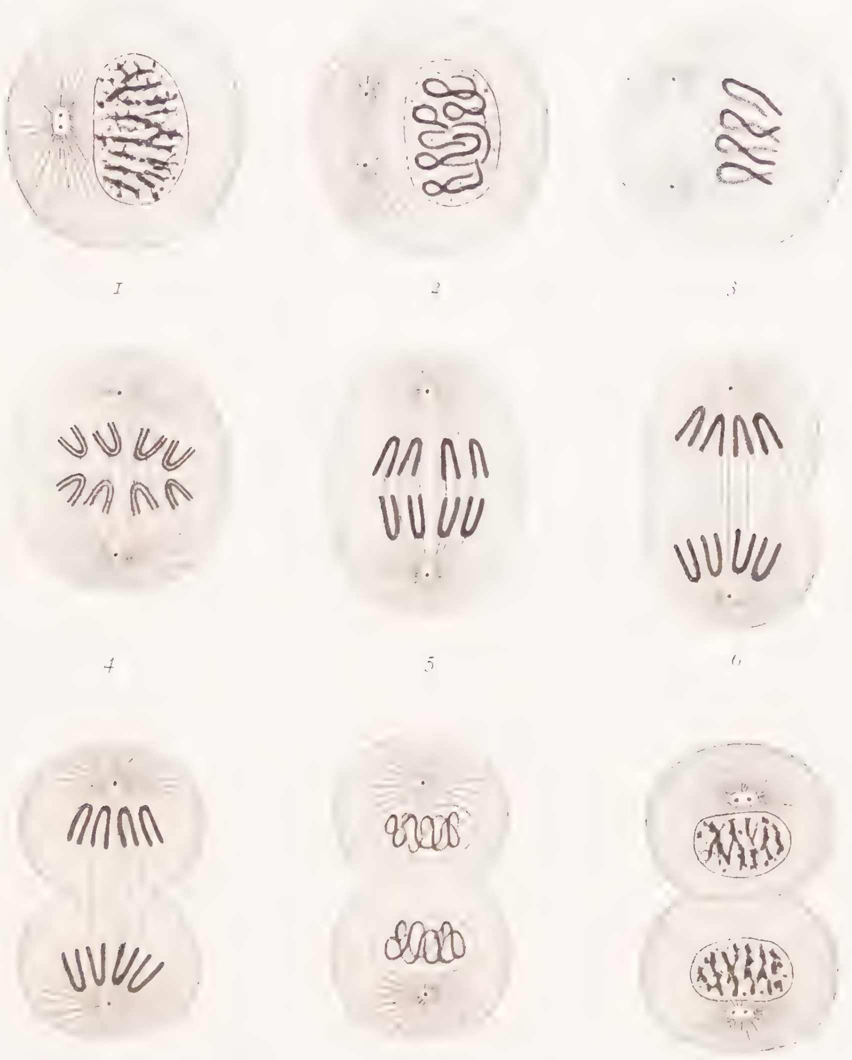

Fig. 2

It is not the division of the cytosome, nor even of the nucleus as such, for which Nature is striving, but the division of the individual chromosomes; the biological significance of which will be discussed later.

As to the centrosome it has already been mentioned that in cells which divide rapidly a number of times the centrosome may divide even during the resting stage of the nucleus and form a diplosome (p. 13). When this is the case the two monosomes of the diplosome move apart and between them achromatic threads appear which show a slightly curved form; later when the daughter centrosomes begin to move apart they form the basis of the characteristic achromatic spindle. If the centrosome is still undivided at the commencement of mitosis, it divides into two during the stage of the close spireme.

Pl. 2, Fig. 3

In the stage of the open spireme the chromosomes are so oriented that the bend in each is turned toward the divided centrosome and the achromatic spindle which is developing in connection with it. The position of the centrosomes marks the so-called polar side of the spireme; the opposite side is known as the antipole, and the free ends of the chromatin loops are turned toward it. As the centrosomes in the polar field gradually withdraw farther from one another two important phenomena are observed. Firstly: there proceeds from each centrosome a protoplasmic radiation whose rays usually reach the surface of the cell; so that each centrosome becomes the center of a system of rays, the astrosphere. Small at first, this system of rays grows larger and larger as the centrosomes separate farther and farther. Secondly: the achromatic threads by which the two centrosomes remain in connection become arranged in a double cone or spindle whose long axis increases with the increasing separation of the centrosomes. The threads of the radiation which proceeds from the centrosomes, are termed polar rays.

Pl. 1, Figs. 3, 7–9, 16

Pl. 1, Figs. 8, 9, 16

Pl. 2 Fig. 4

This fusiform figure quickly increases in size so that of necessity it occupies an axial position in the cell, and with its establishment there is completed the last stage of the prophase. This figure, known as the mother aster or **Monaster,** is one of the most characteristic features of the whole process of mitosis and will be described at once; afterward its derivation from the open spireme will be discussed. In the figure a distinction must be made between the achromatic and the chromatic elements composing it. The chromosomes represent the latter; they are arranged in a circle around the equator of the spindle and form the EQUATORIAL PLATE of the figure. The chromosomes are disposed in such fashion that the bend of each is turned inward toward the axis of the spindle; while the free ends are turned outward and away from it. If such a karyokinetic figure is viewed from one of the two poles of the spindle (polar view) the chromosomes, arranged about the equator as described, form a starlike figure, the monaster. It is to be understood that the circle of chromosomes does not lie in an exact plane, or even nearly so; in particular the free ends of the chromosomes incline toward the poles to a considerable degree (p. 28).

Pl. 2, Figs. 2, 4

The achromatic portion of the figure in the monaster stage of mitosis is represented in the first place by the achromatic spindle. This has the shape of a quite regularly formed double cone whose apices are the centrosomes. The latter are often decidedly enlarged at this time, and between them are stretched the achromatic fibers of the spindle. Two groups of these may be distinguished; the fibers of one group extend without interruption from one centrosome to the other and are called CENTRAL SPINDLE FIBERS, while the part of the figure formed by them is termed the CENTRAL SPINDLE. The fibers of the second group composing the spindle are those which proceed from both centrosomes and terminate on the chromosomes of the equatorial plate; they are called TRACTION FIBERS or MANTLE FIBERS.

Pl. 2, Fig. 3

The relation between the two kinds of spindle fibers is such that the central spindle fibers, as the name implies, form the spindle in the center of the figure; while the traction fibers are placed around it and form a conical mantle — hence the name of mantle fibres. Ordinarily the number of the latter is much greater than that of the central spindle fibers; and in addition they are usually much finer. Thus to each chromosome lying at the equator there go from both poles a number, and usually a rather large number, of traction fibers. In the usual form of the chromosomes these are inserted on that surface which is turned toward the pole; so that by means of the traction fibers each chromosome is in connection with the two centrosomes lying at opposite poles of the spindle. The number of traction fibers which go from each pole to a chromosome is the same, although it varies in different forms of cells; under certain circumstances it may amount to 24 but occasionally is less. They are not always attached to the whole length of the chromosome, often they are lacking at the free ends so that they act only on the bent portion of the chromosome.

Pl. 1, Fig. 12

The polar radiation also belongs to the achromatic constituents of the karyokinetic figure in the monaster stage. About this time the radiation as a rule reaches its maximum size, so that the rays of the two astrospheres cross in the central plane. Naturally this is true only for very small cells. Often these rays appear only in very delicate form.

The origin of the achromatic substance of the karyokinetic monaster is still uncertain. The central spindle fibers appear to be formed directly from the centrosome, and the polar rays perhaps develop from the cytoplasm under the influence of the same structure. It is difficult to decide whether the mantle and traction fibers (and the central spindle?) arise from the achromatic substance of the resting nucleus as it disintegrates, or whether they form quite independently of the previous nucleus; the question is as yet unsettled. It is equally possible that just as the nuclear sap mixes with the cytoplasm, the nuclear membrane and the linin framework may also simply dissolve in it.

The change from the loose spireme to the monaster as above described appears to take place relatively quickly; for while in an area where mitotic divisions are occurring there are numerous spireme stages to be found, and those of the monaster are even more abundant, transition stages are rare. Observation of these intermediate stages shows that while the central spindle is elongating there develope the mantle fibers, which previously were lacking. These become attached to the chromosomes which are already oriented with reference to the pole, and gradually draw them into the equatorial plane of the enlarging spindle. At the beginning of this process the spindle still lies eccentrically as regards the chromosome spireme. By the growth in length of the spindle it is forced more and more into an axial position, which materially lightens the work of the traction fibers in drawing the chromosomes to its equator. That this is not an easy task appears from the fact that frequently at the beginning of the monaster stage one or more chromosomes are found distant from the main body; that is, certain of them have not yet been moved to the equator of the spindle by the traction fibers. With the establishment of the monaster the preparatory stages of mitosis have reached their objective. There ensues for the process as a whole what might be termed a pause for rest. Before studying the further steps of the process which begin with the so-called **metakinesis,** it should be recalled that each chromosome has a longitudinal cleft which may remain latent until the monaster stage, but occasionally is in evidence as early as the spireme. The spindle fibers which are inserted on the chromosomes are termed traction fibers, because they are assumed to be able to shorten and draw those parts of the chromosomes to which they are attached nearer to the centrosome from which the fibers proceed. The assumption that these fibers can actively exert traction, is assailed on many biological and physical grounds; but it is widely accepted and is followed here because it renders simple the presentation of the process. It has already been seen how these fibers can drawn the chromosomes of the spireme to the equator of the spindle.

Pl. 2, Fig. 3

Once the chromosomes are in this position the longitudinal cleft becomes evident and a shortening of the traction fibers occurs which separates the two daughter chromosomes along the line of the cleft and gradually moves them toward the poles. The separation of the daughter chromosomes, for which the term metakinesis is used, does not at once involve the entire length of the chromosomes; but the daughter chromosomes separate from one another first at the region of the bend, and only when this separation has advanced to a certain point do the free ends part company. This stage begins the so-called **metaphase** of the process of karyokinesis.

Pl. 1, Figs. 12, 17, 18

Frequently the first changes in the cytosome itself begin during metakinesis as a change in the form of the cell due to its elongation. Naturally in this change the form of the whole cell and the location of the spindle both play a part. The spindle takes its position from the shape of the cell, having regard to cell inclusions of paraplasmic nature (p. 5). In spherical cells the spindle may lie in any diameter whatever. In elongated cells the axis of the spindle is placed in the long axis of the cell; in cells containing inclusions, such as yolk, it lies in the long axis of the greatest accumulation of protoplasm. But the form of the cell as a whole does not always begin to change with the onset of metakinesis; frequently the cytosome lengthens only when metakinesis is almost or quite completed.

Pl. 1, Figs. 13, 14, 18 It may be repeated that the action of the mantle fibers makes evident the longitudinal cleft in the mother chromosome and causes a part (the daughter chromosome) of each one to move toward the corresponding pole of the spindle. This is equally true for all the daughter chromosomes, consequently they form two asters which move apart. At first the individual chromosomes of the asters slope in such fashion that they lie nearer together at their free ends than they do at the points of bending. However the traction of the mantle fibers is working constantly and rather quickly; so that, as the asters separate, they are drawn into parallel positions and in this arrangement come close to the poles of the spindle. This forms the typical picture of the **diaster** and marks the close of a definite stage of mitosis. The figure persists for a time and with it begins the stage of the **anaphase.**

In areas where mitosis is in progress the picture of the diaster is next in frequency to that of the monaster, and is almost as common. It is characterized by a notable elongation of the whole mitotic figure, always accompanied by a lengthening of the cell. Further than this the form of the spindle is not essentially changed. After the shortening of the mantle fibers the equator of the spindle disappears as such; only the central fibers are visible in the interval between the two asters. These fibers now run almost parallel courses, or show a slight curving like barrel staves. They are now termed connecting fibers, for they alone join together the two asters. To this cask-shaped figure are applied, like top and bottom, the distinctly arched asters. The latter are now joined to the centrosomes by the shortened traction fibres, which being set close together give to the flatly-conical ends of the figure a quite finely striated appearance. This is in contrast to the coarsely striated look of the middle region of the spindle, which even yet is formed of the central fibers now termed connecting fibers. The polar radiation is little changed; naturally the two astrospheres move apart as the cell lengthens, and in consequence their rays no longer touch or intersect at the equator.

Pl. 1, Figs. 13, 14, 18 As the two daughter asters approach the centrosomes very closely the first ringlike constriction of the cytoplasm usually begins to be noticeable. It is situated just at the position of the former equatorial plane of the mitotic spindle. The connecting fibers which until then were slightly curved now straighten out completely and lie exactly parallel. The further course of the process is just like that by which the monaster was formed from the spireme, but naturally in the reverse order. A daughter spireme is formed which at first is open, then a nuclear membrane forms, followed by a linin framework; and each close daughter spireme becomes the nucleus of a corresponding Pl. 1 Figs. 14, 19 daughter cell. In this last step the chromosomes pass in reverse order through the same changes as were observed in the transformation of the mother nucleus into the close mother spireme. During the transformation the figure is known as the **dispireme.**

While the daughter asters are developing into daughter nuclei, as has just been briefly outlined, there occurs the final division of the cytoplasm, which in contrast to the nucleus passively suffers constriction into two parts. Naturally, now that the work is finished, the kinetic apparatus of the cell ceases activity. The polar rays disappear, and the traction fibers suffer the same fate when they have played their part. Usually the connecting fibers, the remnants of the central spindle fibers, are to be observed somewhat longer. Often their remains are to be recognized joining the two daughter cells, should the plane of division be visible throughout its whole extent. In such case they appear as a bundle of fibers caught together almost in the middle and crossing the plane of division; but soon afterward they degenerate. If the centrosomes enlarged, and they commonly do so at the height of the process (monaster), their size now diminishes. Pl. 1, Figs. 15, 19, 20

Now occurs the final division of the former mother cell into the two daughter cells. Each has received through simple constriction one half of the cytoplasm, and each contains one of the two centrosomes; while the nuclei of the newly formed cells are derived from the nucleus of the mother cell, but not, as is the cytoplasm, by the method of constriction. It is not the nucleus as such which is halved, but its chromosomes; for they are split from end to end. It must be concluded that the achromatic constituent of the nucleus, which at the beginning of mitosis simply dissolves in the cytoplasm and in the reconstruction of the daughter nuclei is formed anew, must have special significance for the economy of the cell; but it must also be quite subordinate as regards its reproduction. The best clue to the complicated process of the formation of the chromosomes from the nuclear network, and their rather ceremonious method of division, lies in the process of fertilization; for in it may be observed the fusion of the two germ cells, male and female. Not only the morphology of this process, but observations upon cross-fertilization and others of an experimental nature, have all yielded evidence that the chromosomes alone are the bearers of heredity; in which matter neither cytoplasm nor centrosome play any part.

When there occurs within a tissue (*i. e.* within a formation consisting of similar cellular elements) an increase in the number of cells, the character of the new cells must be the same as that of the mother cells which divide. If the chromosomes are the bearers of heredity the same characteristics will reach the daughter cell as were possessed by the mother cell, should each bearer of the hereditary qualities be divided in such fashion as are the chromosomes; but not if the mass of chromatin is arbitrarily divided as it is in direct nuclear division. Corresponding to the structure of the chromosomes as already described (p. 27) this division must be a longitudinal one. Only thus can it be guaranteed that the daughter cells will be exactly the same as their mother cell, and consequently as the remaining cells of the tissue. The mechanism of mitosis, which appears so unnecessarily complicated, is thus a necessity for the production of daughter cells of like habitus as the mother cell. In addition it also guarantees the maintenance of a constant number of chromosomes (p. 22).

Reference has already been made briefly to the fact that in many animals there are found chromosomes differing in length or thickness, and as a result recognizable from external appearance alone as bearers of presumably different hereditary characteristics. This fact explains the necessity of a longitudinal division of chromosomes in general.

Certain facts would indicate that chromosomes possess not merely constancy in number but also individuality, in the sense that identical chromosomes appear in successive divisions. Briefly these facts are: the longitudinal division of chromosomes; their equal distribution to the daughter cells in such a way as to maintain a constant number in each cell; that this number is maintained from generation to generation of cells; that when cells containing chromosomes of different form divide, each generation of cells receives chromosomes not merely to the same number, but also of the same form. These facts imply that chromosomes persist as independent individuals during the resting stage of the nucleus between one cell division and the next; although in their structure most resting nuclei show little of such an appearance. When after mitosis the chromosomes of the daughter spireme are transformed into the chromatic nuclear network of the resting stage, it must be assumed that in a latent manner the individuality of the chromosome still remains, in the sense that each chromosome has an achromatic covering in which the chromatin proper is enclosed. While during the resting stage the chromatin passes out of this envelope, at the beginning of a division the chromatin which has been distributed in the nuclear network slips back, so to speak, into its shell.

When a cell has divided by mitosis into two daughter cells naturally at first each Pl. 1, Fig. 20 is about half as large as the mother cell. Newly formed daughter cells can be recognized among the neighboring cells of a tissue by their smaller size; furthermore they have not as a rule entered so completely into the community of cells as not to betray their youth through being placed markedly opposite one another. Between them lies the earlier plane of division of the mother cell. The cells soon increase in size; the cytoplasm grows and to a corresponding degree the nucleus does the same. If the other cells of the tissue possess a diplosome during their resting condition (p. 13) the centrosome of the young cell also divides. The nuclear network forms within the nucleus, becoming finer and finer the longer the resting stage lasts. Basichromatin passes more or less clearly into oxychromatin, and most noticeable of all, one or more nucleoli are formed. Thus in a short while the two daughter cells attain the full size of the mother cell and are no longer to be distinguished from the remaining cells of the tissue. These last changes represent the definitive close of the process and together constitute the **telophase** of karyokinetic division. Thus in mitotic-karyokinetic division there are four successive phases to be distinguished: prophase, metaphase, anaphase, and telophase.

The variety of mitotic division described above is known as EQUATION DIVISION because the chromatin in each chromosome is equally divided between the nuclei of the daughter cells. In the maturation of the sex cells the number of the chromosomes must be reduced by one half; otherwise upon fertilization, *i. e.* the fusion of male and female sex cells, the number of chromosomes would be doubled. The reduction of the number of chromosomes occurs by a REDUCTION DIVISION in which the traction fibers no longer cause the separation of half-chromosomes but of entire ones which had previously become joined. Cells or nuclei which contain the unreduced number of chromosomes are called DIPLOID, those whose chromosome number has been reduced to one half are termed HAPLOID. The chromosomes in joining, or conjugating, pair off and the members of a pair unite end to end. Consequently in the reduction division these chromosomes are not cleft lengthwise but the separation occurs by a cross-cleavage.[1]

While the process of mitosis is usually investigated in fixed preparations it is possible to study it, at least in part, in living objects. The rapidly growing larvae of the tailed amphibia have large cells and are particularly suitable. The mitoses of cartilage cells in the gill cartilages of salamander larvae are especially easy to study under the microscope since the cells are isolated and lie in a very transparent substance. The behavior of the chromosomes in the chief phases of mitosis can be clearly seen. Especially it can be recognized that in the apparent pauses for rest during the process, for instance at the height of the monaster stage, there is movement taking place in the preparation. In this case it is a rhythmic movement toward one another on the part of the chromosomes of the equatorial plate. With relatively long pauses the free ends of the chromosomes approach and again separate, which causes the circle of chromosomes to appear now thicker, now thinner; a picture which corresponds throughout to the appearance of the chromosomes of the equatorial plate in fixed preparations.

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[1] Fusion side by side seems also to occur, followed by a longitudinal cleavage. — Trans. Note.

In a similar manner the duration of the process of mitosis has also been determined. In cold blooded animals it continues from one to several (5) hours before the daughter cells are formed, according to the temperature; while in warm-blooded animals it requires from one quarter to one half of an hour.

The Duration of the Life of Cells and Their Death

In duration of life the individual cells of the human body differ greatly; there are short-lived cells and others of extraordinarily long life. Examples of the first are the red blood cells whose life is of but a few weeks duration; while the nerve cells are extremely long-lived and under normal conditions last as long as the organism itself.

Beside the short-lived red blood cells there are in the body many other cells which live but a short while; consequently throughout the whole life of the human body it is quite normal for cells to be dying. Within the living organism many cells die each day, indeed for the normal course of the life processes of the organism as a whole, such death of cells is absolutely necessary. This fact shows most plainly that within the body each cell leads a more or less independent existence.

It is remarkable that the death of cells is accomplished without any appearance of violence, at least not normally. Usually it is rather difficult to detect dying cells; in many cases their death occurs, so to speak, in secret. Wandering cells lead an independent life so long as they traverse the tissues proper; but when they leave these and pass through superficial epithelia, they die. This occurs particularly in the intestine and also in the mouth cavity; it is a perfectly normal process and all life long is in continual operation.

The process of secretion is often connected with the death of the secreting cells as in holocrine secretion (p. 43). The cells of the intestinal epithelium secrete mucus and Pl. 4. Fig. 3 die in the process, as also do those of the cutaneous sebaceous glands; for these cells secretion involves death. In the formation of the enamel of the teeth, the death of the cells which produce the enamel is invariable.

In the discharge of the female sex cells, the eggs or ova, from the ovary numerous cells are also discharged which die and disintegrate in the oviducts. The so-called polocytes or polar bodies of the egg cell are also destined to die; and the female sex cell itself, the ovum, suffers the same fate if it is not fertilized. To a very great extent the same Pl. 71. Fig. 5 is true of the male sex cells which die in millions, and in the case of many animals even billions, in the discharged semen.

The morphological appearances which normally accompany the death of cells are not always the same. The first signs of approaching death are usually to be recognized in the nucleus which shrivels, squeezes out its nuclear sap and grows visibly smaller, at Pl. 4, Fig. 3 the same time losing its normal structure. It now stains evenly dark with basic dyes and usually its contour shows points and notches. This PYCNOSIS of the nucleus is always Pl. 92, Fig. 7 an indication of impending death. It is commonly followed by the destruction of the nucleus through a so-called karyolysis or chromatolysis; *i. e.* the pycnotic nucleus breaks up into fragments or droplets which gradually lose their staining power and then slowly dissolve. These processes are to be observed very clearly in the disintegrating follicular epithelium which has been discharged from the ovary along with the ovum.

The behavior of the cytoplasm varies greatly according to the manner of death of the cell. In holocrine secretion it is entirely, or almost entirely, used up in the formation of the secreted material, as in the case of the cells of sebaceous glands; so that after the pycnosis and disappearance of the nucleus nothing more remains of the cell. Or as in the case of the secretion of mucus in goblet cells, the small part of the cell remaining may be visible for a time wedged in between its neighboring cells; then it slowly and almost without notice disappears. After death the red blood cells, which in mammals are non-nucleated, break up into fragments which are phagocytosed by other cells.

Certain cells such as those of the epidermis of the skin meet death through cornification; *i.e.* their cytoplasm is transformed into the horny substance keratin, and at the same time the nucleus disappears. Hair, nails, etc. consist of masses of such dead, cornified cells.

The fact that in the normal life of the body numerous cells are regularly and continually dying involves the need of providing substitutes for them. Since cells can arise only from cells, and since the normal method of the increase of cells is by mitotic division, it follows that in all places where cells are continually dying the appearances of the mitotic division of nuclei and cells must and can be observed.

The Connections between Cells

Since only a few of the many kinds of cells in the body are free and without mutual connections, the vast majority of cells are in contact one with another; although there are tissues whose cellular elements for the most part do not meet, being separated by other tissue elements, as in connective tissue. But as connections between cells are the rule in the formation of tissues some survey of them must be given here, though many of their peculiarities will be discussed only under the individual tissues.

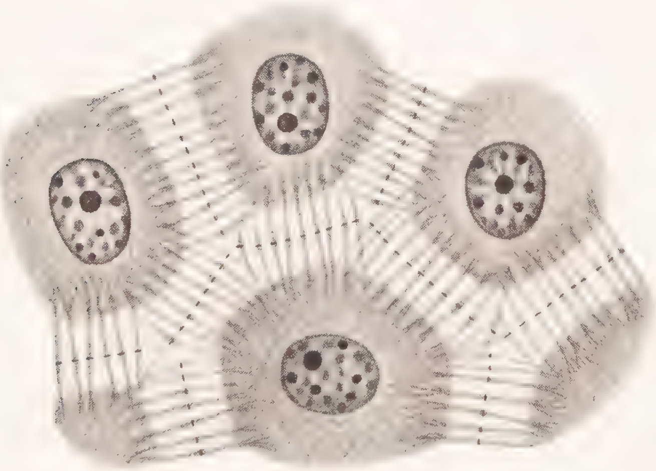

Fig. 3. **Diagram of Intercellular Bridges.**

Four entire cells are seen and parts of two others. The intervals between them are crossed by intercellular bridges. Midway in the latter are seen nodelike thickenings with cement lines indicating the limits of the cells.

As a rule two different types of connections between cells are to be distinguished, those PER CONTIGUITATEM and those PER CONTINUITATEM. In cases of the first type, such as with relatively few exceptions occur among epithelial cells, the cells lie with their adjacent surfaces close together and adhere to one another by a so-called CEMENT SUBSTANCE, which usually is present in only very small
Pl.3, Fig.6 amount. This cement substance is homogeneous and structureless; and may easily be de-
Pl.59, Figs. 2, 3 monstrated by treatment with a solution of silver nitrate, which causes silver chloride to form in the cement; the action of light then reduces the chloride to silver which appears black. The cement extends only as far as does the cytoplasm; *i.e.* to the base of the cuticle, where commonly it ends by expanding slightly to form the so-called terminal bar (p. 39 and *Fig.* 6). The surfaces thus cemented together are not necessarily plane

surfaces; on the contrary they are frequently curved or even marked by pronounced grooves, etc.

Pl. 3, Fig. 13 Intercellular bridges such as occur between many epithelial cells also belong in the category of cell connections by contiguity. In this case the opposed surfaces of the cells do not lie in immediate contact, but between them there remains an interval filled with fluid and crossed by fine threadlike bridges which run from cell to cell. The first impression is that the bridges are anastomosing processes and constitute a connection by continuity. Closer examination shows midway in each bridge a thickening, like a node; and each node may be resolved into two half-nodes united by cement. The intercellular bridges are merely thickened continuations of the fibrils of the cytoplasm; consequently where they terminate in the half-nodes mentioned above, the cell from which they arise also terminates, and a new cell begins united to the former by cement (cf. *Fig. 3*). Between the intercellular bridges, and separated by them are found the intercellular spaces.

By the connection of cells **per continuitatem** is understood the occurrence of direct connection between neighboring cells through their processes; usually the latter are very fine and the cells some distance apart. In this manner there are formed **cell nets**. While connections by contiguity are realized in epithelial tissues, cell nets of pronounced form occur in supporting or connective tissues. These anastomotic connections of neighboring cells are almost always multiple; it is not that just two processes, one from each cell, should meet but as a rule there are a number of such pairs. Nor does a cell connect in such fashion with **one** other cell alone but with several neighboring cells. Since the anastomosing processes of the neighboring cells pass directly into one another this manner of cell connection, to express it with strict logic, makes of the cells a true syncytium (p. 14). However since these cell nets differ essentially in general habit from the true syncytia, which are compact masses of protoplasm, they are not included under this concept. The name "cell net" corresponds much better to their whole appearance; the cells of the net are said to stand in connection by continuity.

Non-cellular, Secondary Constituents of the Human Body

It was stated at the beginning of this chapter that the body is constructed of cells, that originally in the embryo only cellular elements are present, but that gradually, in the course of development non-cellular constituents become demonstrable. However these arise from cells or at least are formed through their active participation. The cells represent the smallest structural elements that lead independent lives, but no such statement can be made about these secondary elements for they fail to show the phenomena of life described for cells; among other things they cannot by their own action reproduce or increase their numbers.

The structural elements in question are of the nature of **fibers**; *i. e.* threadlike structures, wholly or partly independent of the cells. They lie between cells like an intercellular substance and may either occur singly or be arranged in bundles. They show no internal structure but are homogeneous throughout and hence are known as **elementary fibers**. They are not to be confused with fibrous differentiations within the cytoplasm of cells or of syncytia, although genetically they are closely related. For, with possibly some exceptions, they were not at first independent but in their earlier stages of differentiation were intracellular, or at least were enclosed in an exoplasmic layer of the cytosome (p. 62).

The above statements apply to the fibrous elements of supporting or connective tissue and perhaps also those of neuroglia (see nervous tissue); but not to the fibrils of muscular tissue nor of nervous tissue in the narrower sense.

Fibers such as the above may by partial fusion form **ELEMENTARY MEMBRANES** like the fenestrated membranes of the walls of the larger arteries (p. 60). In the same way the so-called basal membranes, hyaline membranes etc. are non-cellular and consist of elementary fibers woven together like a felt.

Finally the cement substances between cells are also secondary, non-cellular constituents of the body; as also are many cuticular structures such as the oölemma of the ovum. The enamel of the teeth is not a cellular structure but a secretion product of cells which have disintegrated and left it an independent cuticular formation.

Compared to the cells these elementary fiberlike constituents play a subordinate rôle in spite of the great bulk which they present in many kinds of tissue; a bulk which, as in many varieties of connective tissue, may greatly exceed that of the cells themselves.

II. The Tissues, Histology Proper

Tissues are formed when cells of similar form and similar embryological origin are assembled in regular arrangement, or when the same takes place with the secondary constituents of the body, the fibers. Or to express this concept in the form of a definition: tissues are composed of large numbers of similar cells with, or without, the addition of fibrous elements, the structural elements being regularly arranged.

Thus there are tissues which consist only of cells, and other tissues in the formation of which both cells and fibers are concerned.

Four tissues can be distinguished in the human body.

I. Epithelial tissue.
II. Supporting or connective tissue.
III. Muscular tissue.
IV. Nervous tissue.

Epithelial Tissue

Epithelial tissue is, so to speak, the fundamental tissue of the human body in as
Pls. 3, 4 much as it proceeds directly from, and in various ways retains the primitive character of, the lamellae of the three germ layers. The cells of these lamellae are arranged in the manner of an epithelium, but the epithelia of the fully developed body show one outstanding difference; they always rest upon a basis of connective tissue, a basis which is absent from the germ layers. The cells of the germ layers are columnar in form (p. 1) and have two free surfaces, while their lateral faces are united to those of neighboring cells by cement substance. On the other hand the cells of epithelial tissue have one free and one basal surface (p. 33). In addition many kinds of epithelium differ from the embryonic epithelium-like lamellae of the germ layers by becoming eventually epithelia of many layers of cells; while the embryonic germ layers represent an epithelium of but one layer of cells, or in extreme cases of a few layers.

Of all the tissues epithelia show least departure from the conditions in the germ layers; the others before their specific differentiation first pass through an epithelium-like stage; this is especially the case with most muscular tissue and with nervous tissue as a whole.

EPITHELIAL TISSUE IS COMPOSED OF CELLS ONLY; as a rule neither syncytia, nor fibers play any part in its formation. The connections of the cells of epithelial tissue — apart from rare exceptions — are by contiguity, mostly through cement substance, rarely through intercellular bridges (p. 31). Without exception epithelial tissue is devoid of blood vessels. Although in rare cases it may appear as if blood vessels actually had pressed their way into an epithelium, such an appearance is deceptive.

Epithelial tissue is widespread in the human body. As epidermis it covers the surface of the skin; it also covers the mucous membranes of the intestines, nasal cavity, and the passages of the respiratory and genito-urinary systems; it lines the serous cavities[1] and forms the parenchyma of the true glands. In the latter case it may form considerable masses of tissue, as for instance the liver.

Considering first the **superficial epithelia** such as cover the skin, mucous membranes and inner surfaces of the serous cavities, epithelial tissue appears in its least complicated form and most resembles the embryonic germ layers when it consists of but a single layer of cells. Such an arrangement is named a SIMPLE EPITHELIUM. The cells in such cases are always united by cement substance and are PRISMATIC in form, being uniformly regular, six-sided prisms, rarely five-sided. But the height of the prisms varies greatly, some are several times as high as they are thick, others are very low or even flat. The bulk of individual cells may indeed vary, but is constant within certain limits, as a result the long prismatic cells are slender, while the short or flat prismatic cells cover the greater area.

There are all gradations between high prismatic cells and those which are quite flat. The former have long been known as columnar cells, and the terms COLUMNAR, Pl.3, Fig.6
CUBICAL and SQUAMOUS EPITHELIA have arisen because of the forms of the component Pl.4, Fig.9
cells. The varying height of the prismatic cells of a simple epithelium is not fully indicated by these three terms, but a further compounding such as high columnar, columnar, low columnar, cubical, low cubical and squamous will sufficiently distinguish the chief forms. It must be left to individual choice whether a given cell is to be described as, say, low columnar or cubical. Within the same epithelial covering the height of the prismatic cells may increase or decrease often to a considerable degree, high columnar cells may become low columnar and cubical cells may gradually become squamous.

All simple epithelia whether high columnar or squamous have one common characteristic; they are prisms with level bases and rest on a foundation of another kind of tissue, namely connective tissue, in such a way that in all the cells a basal and a free surface can be distinguished. By contrast the lateral surfaces of the prisms which are fastened together by cement do not at all need to be smooth but are often decidedly grooved. It is not probable that there is any connection between the prismatic cells of simple epithelia other than the cement; although many investigators describe in addition the occurrence of intercellular bridges between the squamous cells of the serous membranes. The quantity of cement is usually very small, but in simple squamous epithelium may be markedly increased so that occasionally small masses of cement are seen.

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[1] It is quite incorrect to characterize the epithelial lining of the serous cavities as endothelium. On this point see below, and p. 94 under "Endothelium".

The free surfaces of many simple epithelia present special devices such as cilia or a cuticle, but since the same are found on the surface of stratified epithelia they will be discussed in detail later on; the same applies to the terminal bars of the cement (p. 39).

In covering a convex surface the longer the form of the cells of a simple epithelium the more must their basal part be narrowed until they are no longer columnar but have become more or less conical, or better pyramidal. Where strongly and sharply curved
Fig.4 surfaces are to be covered this basal tapering of the cells is often extreme.

It must also be borne in mind that epithelial cells are by no means rigid and hard but like all cells are quite pliable structures which react markedly to pressure etc., so that the height of the epithelium of a distensible hollow organ is greatly decreased when the organ is filled and the wall is correspondingly stretched. In such cases it is usually a stratified epithelium which is involved, and the number of rows of cells diminishes with the flattening of the epithelium and increases when conditions are reversed.

Pl.3, Fig.2 As regards the occurrence of simple epithelia, **simple columnar epithelium** with
Pl.4, Figs.4,5 striated cuticle is found as the epithelium lining the intestines both large and small; in
Pl.45, Fig.2 height the cells vary from low to high columnar. Epithelium of similar appearance is
Pl.47, Fig.7 observed only in the gall-bladder and bile ducts; without the cuticle it forms the lining
Pl.52, Fig.1 epithelium of the stomach and of the ducts of many glands. The epithelium of the sur-
Pl.49, Figs.2–4 face of the ovary, the so-called germinal epithelium is low columnar without cuticle.

Pl.70, Fig.1 When the surface of an epithelium such as the above bears cilia the term usually employed is SIMPLE COLUMNAR CILIATED EPITHELIUM. The epithelium of oviduct and uterus is of this type; beginning as low columnar in the oviduct, it passes through columnar and becomes high columnar in the cervix uteri. Simple low columnar ciliated epithelium is found in the finer branches of the bronchial tree, the so-called bronchioles, and on the mucous coat of the accessory nasal cavities. In the middle ear the epithelium is cubical or flat-cubical, partly with and partly without cilia; and in the accessory cavities of the middle ear it flattens into an extremely squamous type. Simple flat-cubical epithelium occurs as the epithelium of the lens of the eye, and as mentioned above in part of the
Pl.3, Fig.3 middle ear; also in places in the membranous labyrinth and in the ducts of numerous
Pl.4, Figs.7,8 glands. The flat-cubical pigmented epithelium of the retina must be given a place by itself midway between epithelial and nervous tissue; while the high cubical to low columnar epithelium of the venous plexuses of the brain must properly be ranked with the
Pl.73, Fig.2 nervous tissues, but as retaining its embryological character.

Simple squamous epithelium, also known as pavement epithelium, occurs as the epi-
Pl.80, Figs.1,6,7 thelium of the serous membranes although in these situations it does occasionally pass from true squamous to flat-cubical and may even attain a columnar form on the ovary,
Pl.3, Fig.6 particularly during embryonic life (p. 33; it is NOT an endothelium). The epithelium of
Pl.4, Fig.9 the mastoid cells is very flat, as is also that of the intermediate ducts of the salivary glands
Pl.45, Fig.2 and of the pancreas. The epithelium of parts of the membranous labyrinth is flat and that
Pl.53, Fig.6 lining the alveoli of the lungs is extremely so, and partly without nuclei as well. The cell
Pl.59, Figs.2,3 boundaries of the simple squamous epithelia may be straight and the surfaces even, but very commonly the boundaries are wavy as may be shown by blackening the cement with silver nitrate.

It is evident that the **stratified** forms of epithelium must be more complicated in their structure than are the simple. By stratified epithelia in the narrow and proper sense are understood those epithelia which consist of at least two layers of cells; one of these is basal, resting on a membrana propria of connective tissue, the other forms the free surface of the epithelium. In such an epithelium the cells of the superficial layer have no basal surface, nor do those of the deeper layer reach the free surface; the cells of the two layers, as well as of each individual layer are connected by cement. Of this type is the so-called stratified columnar epithelium which usually consists of a flat-cubical basal layer and a superficial layer which is cubical to high-columnar. The free surface may bear a cuticle, stereocilia, or kinocilia (q. v.) and terminal bars may be present. Pl.3, Fig.4

To be designated a **stratified columnar epithelium** it is sufficient that the cells of the superficial layer be more or less columnar, those of the other layers need not be so. Such an epithelium with two layers of cells occurs on the conjunctiva of the eyelid, and in the Pl.66, Fig.8 ducts of sweat and salivary glands, also on the mucous coat of a part of the male urethra, Pl.67, Fig.3 with stereocilia as the epithelium of the ductus epididymidis, and with kinocilia in the ductus deferens. In the last two cases the epithelial cells are perhaps not so much in two layers as in a double row — a pseudostratified epithelium.

Stratified squamous epithelium is a very typical and at the same time an extremely common form of stratified epithelium. It consists of more than two layers, usually of several, but yet is quite typically stratified; so that it affords the thickest and most resistant Pl.3 Fig.1 epithelial coverings known in the human body. Prismatic cells which range in height Pl.4, Fig.1 from columnar to quite flat participate in its formation. The rule holds that the deepest Pl.42, Fig.4 or basal layer is formed of columnar cells, that shorter and shorter prismatic cells then Pl.43 succeed and that the squamous cells form the superficial layers of the epithelium. Pl.44, Fig.1

The flattened, superficial cells of the epithelium are united by cement substance, and many others as are also the basal columnar cells. But the cement often does not reach quite to the base of the latter cells; so that some of the precollagenous fibers, which are woven together to form the underlying basal membrane, project somewhat between the lowermost parts of the cells. Moreover the cells of the basal layer are frequently in a double row; so that only slender processes from the columnar cells of the upper row reach the base of the epithelium. The cells between the upper and the lower layers are most clearly connected by intercellular bridges (p. 31). The squamous cells of the upper rows may become cornified, during which process they die and loose their nuclei.

Stratified squamous epithelium occurs chiefly in two forms. One of these is comparatively thin, with only five layers of cells, a basal columnar, two moderately flattened and two squamous cell layers; the basal surface is parallel to the upper and of even contour. In man this variety is found only as the corneal epithelium. The second variety, Pl.78, Figs.2, 3 unlike the first, is quite common and has a much greater number of cell layers, especially of the squamous cells; moreover the basal surface of the epithelium is more or less deeply indented by conical projections termed papillae which come from the underlying layer of connective tissue. Papillae, and the corresponding invaginations of the basal surface of the epithelium, may in a few situations and for special reasons be wanting; they may also vary extremely in height.

In addition to the cornification of the superficial layers of the cells, which is especially apparent in the stratified squamous epithelium of the epidermis, a number of differentiated structures such as fibrils (tonofibrils) granules, etc. are met with in this variety of epithelium. These will be discussed later on in the chapter.

Stratified squamous epithelium forms the most widespread type of epithelium in the body and is especially to be found where great demands are made upon the epithelium. It may suddenly appear right in the middle of another type of epithelium, like an island so to speak, if the need is sufficiently great. For instance it covers the free borders of the vocal cords of the larynx which elsewhere is covered by a stratified ciliated epithelium. The first mentioned and rarer variety of stratified squamous epithelium is found, as stated, only on the anterior surface of the cornea. The portion of the ocular conjunctiva immediately adjacent shows the same structure; then papillae appear causing basal invaginations and the epithelium becomes gradually thicker. Typical stratified squamous epithelium, the upper layers of which are cornified, is found forming the epidermis of the skin; it also lines the mouth cavity and greater part of the pharyngeal cavity, the whole length of the oesophagus, the vagina and vulva, a portion of the male urethra and usually the entire female urethra; as well as the lachrymal ducts and, as an extension of the epidermis, the external auditory passage. With relatively rare exceptions the basal surface is indented by papillae.

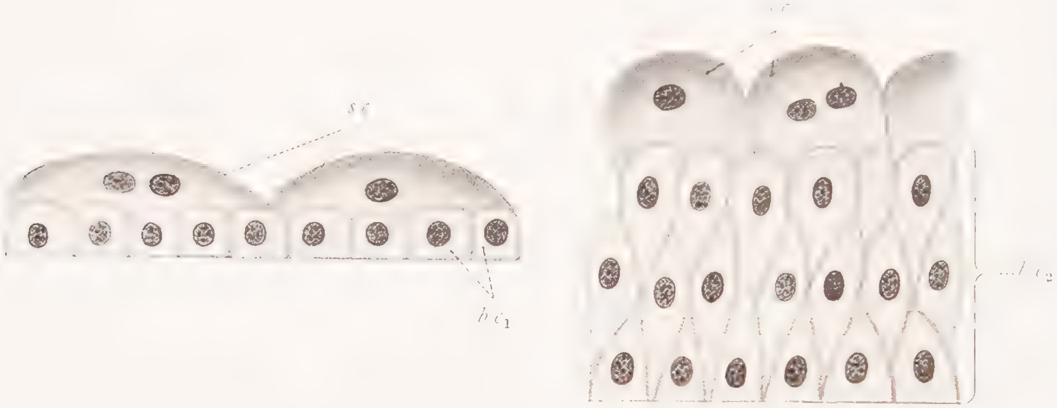

Fig. 4. **Diagram of Transitional Epithelium.**

At the left in distension; at the right in an undistended condition.

s c = superficial cells with crusta-like border
$b\,c_1$ = basal cells
$b\,c_2$ = basal cells in several rows

Fig.4 Another and equally pronounced type of stratified epithelium is the so-called **transitional epithelium.** It would be more appropriately named the epithelium of the
Pl.4, Fig.5 urinary passages (renal calyces and pelvis, ureter, bladder and part of the urethra)
Pl.63, Figs.1–3 for it occurs in them only. To a certain extent it occupies a place by itself, between the
Pl.64, Fig.1 stratified epithelia and those in which the rows of cells are few and not so definitely in layers. In the latter cases all the cells rest on the basal membrane but not all reach the free surface of the epithelium. In transitional epithelium the cells of the superficial layer never reach the basal membrane. They thus form a layer peculiar to themselves. The cells which lie beneath this layer are not truly stratified or at least they are not always distinctly so; nor do all of them as a rule reach the basal membrane. To be exact, transitional epithelium is stratified except in its deeper layers where the cells are in a double or triple row.

This type of epithelium overcomes as does no other the difficulties arising from the expansion and contraction of the organ whose lining it forms; *e. g.* in the empty bladder
Fig.4 it is many times as thick as when the organ is full. If the epithelium is extremely distended the cells of the deeper layers actually form but a single row although in the contracted

state they were in several rows. The cells of the superficial layer never become displaced; when the organ is distended they merely flatten out, and when it contracts they also contract and still form but a single layer. They have a distinct external layer which consequently forms the very surface of the epithelium. This layer resembles a crusta in not being sharply marked off from the rest of the cell (p. 7) although its presence is clearly seen. The cells are large, filled with protoplasm, their surface is more or less arched and each cell has one or two nuclei. Their lower or basal surfaces bear distinct hollows which fit over the tops of the cells of the layer beneath; for each cell because of its great relative size is in contact with two or three cells of the deeper layer. Usually the cells are rather cubical but when extended they become lower, varying from flattened cubical to flat; the depressions in their lower surfaces also become more shallow in the latter condition.

This superficial layer of cells never touches the basal surface of the epithelium even when the basal layer of cells is thinnest during extreme distension, for the latter layer always remains everywhere continuous. Only during most extreme distension do the cells of the basal layer form a single row, otherwise they show most clearly an arrangement in several rows; even when the epithelium is flattened by moderate distension two or three rows may be recognized, and at its greatest thickness this number of rows is more than doubled. In the undistended, or only moderately distended condition it can as a rule be recognized that the cells of the row immediately beneath the superficial cells are longer and almost columnar in contrast to the cells of the more basal rows, which are smaller and usually take a darker stain.

Transitional epithelium shows another special peculiarity. Although a basal membrane is lacking in many glands, this is the only type of epithelium covering a surface which does not rest upon such a membrane but is in immediate contact with the fibrillar connective tissue by its lower surface. As a result the capillary blood vessels lie close to the base of the epithelium, they may even lie between the basal cells enclosed in a small fold of connective tissue and thus give the impression of being intra-epithelial capillaries.

A type of epithelium found extensively is the so-called **stratified ciliated epithelium**, the cells of which however are arranged in rows rather than in layers. This type of epithel-
ium covers the greater part of the mucous membrane of the nasal cavity, the adjacent Fig.5
portion of the nasopharynx, and almost all of the inner surface of the larynx; it lines
the trachea, and the entire bronchial tree as far as the bronchioles (p. 34), also a part of the Pl.3, Fig.7
Eustachian tube (tuba auditiva). This type of epithelium is composed of two kinds of cells Pl.4, Fig.2
one of which forms the general surface of the epithelium and bears cilia, and as a result Pl.55, Figs.2,3
practically determines the character of the epithelium. These ciliated cells have a mark- Pl.57, Fig.3
edly conical shape, not conical in a mathematical sense, but as implying a tapering prism Pl.58, Fig.2
or a long and pointed pyramid. Frequently the point is forked or it may end in a small, Pl.4, Figs.7,8
basal foot-plate. The bases of the cones, fitted closely side by side, form the flat, epithelial surface and bear the cilia; toward the basal surface the cone narrows more or less, according to the thickness of the epithelium. No matter how great this may be, the point, though often drawn out very fine, always reaches the basal membrane. Because of their form these cells leave within the epithelium intervals which become larger toward the basal surface; these intervals in turn are filled by the remaining cells which are often very irregular both in form and in the manner of their arrangement in rows. Beneath them and alternating with them are conical elements which may be quite irregular or of elongated ellipsoidal form. If the parts of the cells which contain the nuclei lie at different levels in the epithelium the nuclei alternate very noticeably; this appearance is quite distinct in the

thicker epithelia. Yet as a whole the cells reach the basal membrane although often with only a slender process.

The cells of this type of epithelium are united by cement but terminal bars are wanting. The thickness of the epithelium varies throughout a wide range, thus within the lung the thickness of the epithelium in the bronchi and their branches speedily diminishes with the diminution in caliber of the air passages. From an epithelium of several rows it diminishes to one of but two rows of cells and finally in the bronchioles to a single row. With the decrease in thickness of the epithelium the height of the ciliated cells also decreases, so that from being pyramidal cells with sharp points, they become at last prismatic cells slightly narrowed toward the basal end.

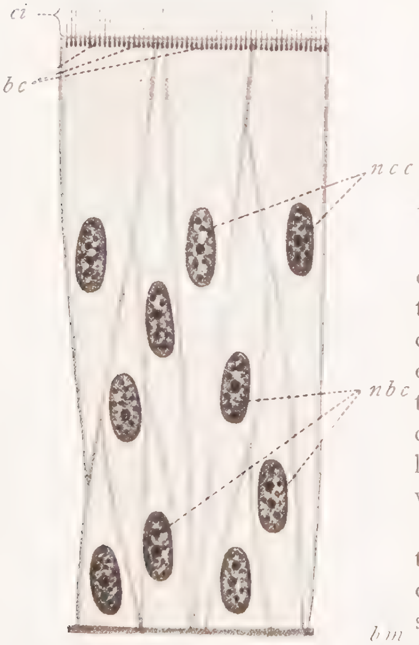

Fig. 5. **Diagram of Stratified Ciliated Epithelium.**

b c = basal corpuscles of the cilia
b m = basal membrane
ci = cilia
n b c = nuclei of basal cells
n c c = nuclei of ciliated cells

Ciliated epithelium such as this with two rows of cells is found in the smallest bronchial twigs (but not in the bronchioles p. 224) and with it should perhaps be coupled the epithelium of the ductus epididymidis and of the ductus deferens (p. 35). But it often approaches the character of a columnar epithelium of two layers of cells since the flat-cubical cells often form a complete layer and prevent contact of the long columnar cells with the basal membrane.

Beside the types of surface epithelium here described there are a number of special arrangements of epithelium connected with many sense organs, which will be described each in its appropriate place. One quite peculiar form in which epithelium occasionally occurs is the so-called **myoepithelium**; for epithelial cells under certain circumstances can become contractile, copy perfectly the form of the smooth muscle cells derived from mesenchyme (p. 99) and assume the functions of muscle. Such muscle cells of epithelial origin, termed myoepithelial cells when in their best differentiated form, are found for example in the wall of the coiled part of the sweat glands of the skin, especially in the larger glands. In this situation their epithelial origin is to be recognized from their position within the membrana propria, and also through the series of intermediate stages between them and epithelial cells. They differ from true smooth muscle cells only in their looser arrangement and, most of all, in not being enclosed in a connective tissue membranella (p. 98). In this category belong also the cells of dilator membrane of the posterior surface of the iris of the eye (q. v.) and the so-called basket cells of many glands (p. 51).

Special Differentiations of Epithelial Cells

Of the special differentiations of epithelial cells the first to be mentioned are the superficial cuticular formations already considered briefly in the enumeration of the various types of epithelium. These are of the nature of partial membranes differentiated by the cell and are less extensively found in man than they are in many animals. The simple columnar epithelium of the intestine bears a quite typical cuticle on its surface, usually spoken of as **cuticular border**. In the living cell it is distinguished from the cytoplasm by having a higher refractive index; and in the stained cell by reacting much more intensely to many dyes. It appears distinctly striated perpendicularly to the surface, a fact which supports the assumption that it is composed of separate and parallel rods united by a kind of cement. This cuticular border varies in thickness according to the stage of digestion or absorption, being distinctly thicker during this process than when the intestine is empty. The so-called BRUSH BORDER borne by many epithelial cells, such as those of the convoluted parts of the renal tubules, is related to the preceding and like it is to be considered as a cuticular formation. It is formed from separate cuticular threads, quite independent of one another and planted firmly on the surface of the cells, like the hairs of a brush. The STEREOCILIA which form a border on many epithelial cells, as in the ductus epididymidis, are of a cuticular nature, and contrast with kinocilia (q. v.). The former are hairlike threads, in length but little less than the cell on which they stand implanted like the short hairs of the brush border. Frequently they are stuck together in bunches though this may be an artefact. In contrast to protoplasmic cilia these cuticular threads are naturally devoid of movement; hence the name of stereocilia.

Pl.2, Fig.7
Pl.3, Fig.2
Pl.4, Figs.3, 5
Pl.52, Fig.1
Pl.61, Fig.3
Pl.3, Fig.4

Striated cuticular border, brush border, and stereocilia are indeed only successive stages of cuticular differentiation of the superficial layer of epithelial cells. While the striated border of the intestinal epithelium plays a part in absorption, brush borders and stereocilia promote the discharge of the secretion produced in their cells and are found only on secreting cells. The kinship of these three types of epithelial cell is shown by the intercellular cement and its terminal bars formed by all of them alike.

As already mentioned (p. 30) the cement which as a rule unites neighboring epithelial cells does not extend between the cuticulae; for instance the cuticular borders of the intestinal epithelium are without lateral connections and project freely into the intestinal lumen, separated only by slight intervals. At the level of the base of the border the cement becomes condensed and as a result stains strongly especially with certain dyes which scarcely affect the cement proper. Since in a sense the cement terminates at these places they have been spoken of as TERMINAL BARS. These surround, as with a frame, the columnar cells just beneath the base of the cuticular border. Since the cells are six-sided prisms their tops, crowned by the cuticle, are held in hexagonal frames which being joined together constitute a network of terminal bars.

Fig.6
Pl.2, Fig.7
Pl.4, Figs.4, 5

Cilia stand rather in contrast to the cuticular differentiations just described, for they display one of the three types of movement shown by animal cells, namely, ciliary movement. Cells whose surfaces bear such a border of motile cilia (KINOCILIA) are termed ciliated cells; and when they form the superficial layer of an epithelium the latter is known as a ciliated epithelium. Cilia are fine smooth protoplasmic threads, which are not merely fastened to the surface of the cell, as is probably the case with cuticular structures, but proceed directly from the cytoplasm of the cell and thus represent threadlike processes of cytoplasm. All those of the same locality are of equal length, which is never great, only a few μ;

Pl.3, Figs.3, 7, 11
Pl.4, Figs.2, 7, 8

indeed their length usually falls considerably short of that of the cell on which they stand. As exceptions there are ciliated cells so flat that the length of the cilia is greater than the depth of the cell beneath them. Except for a very few cases in which they seem to proceed directly from the cytoplasm, cilia are not merely rooted in the cell but spring from ellipsoidal thickenings, the so-called BASAL CORPUSCLES or blepharosomes, which lie close to the surface of the cell. From each corpuscle there projects one cilium, and since one cell bears on its surface a large number of cilia, fifty or even more, depending on the size of the Fig.5 surface, the number of the basal corpuscles is considerable. All the corpuscles lie in the same plane and in sections stain with most dyes more strongly than does the cytoplasm, consequently unless a sufficiently high magnification is employed they produce the im- Pl.3, Figs.3,11 pression of a cuticular border. Under higher magnification this border resolves itself into

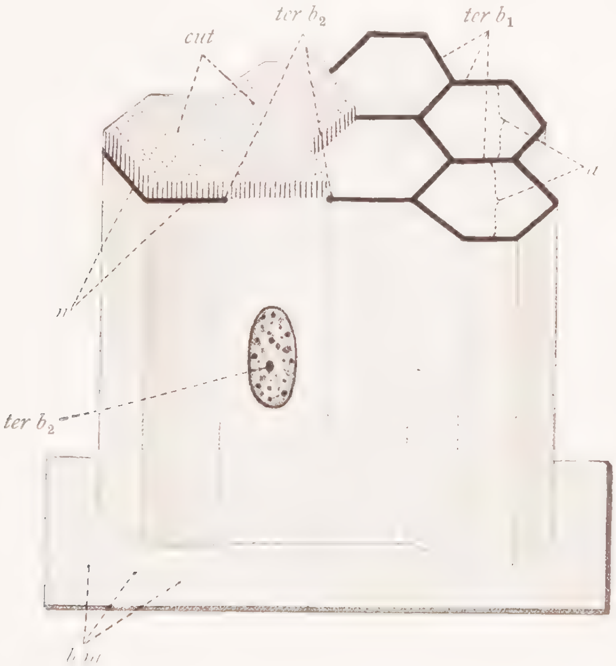

Fig. 6. **Diagram of Simple Columnar Epithelium.**

Seven cells are represented resting upon a basal membrane. The cell on the right is showing three of its six lateral surfaces, the cell on the left shows two, and another cell shows but one. A nucleus is shown in a part of a cell, the remainder of which has been cut away. The cuticular border has been removed from the upper surfaces of the four cells on the right in order to show the network of terminal bars.

a = free surface without cuticular border
b m = basal membrane (membrana propria)
n = nucleus
cut = cuticular border
ter b_1 = terminal bars
ter b_2 = terminal bars cut across

Pl.4, Figs.7,8 the separate basal corpuscles. In contrast to the epithelial cells with a cuticular differentiation, *e. g.* cells with stereocilia, there is no true cuticular border on ciliated cells; nor are terminal bars present. As to the nature of these basal corpuscles they appear to be the centrosomal apparatus in multiple form. While non-ciliated epithelial cells have a simple centrosome, which usually appears as a diplosome and lies close to the cuticular border, or to the surface of the cell; in the ciliated cell the centrosome is broken up into the basal corpuscles. Thus the centrosome plays its rôle as kinetic organ in regulating ciliary movement (p. 13). From the basal corpuscles there proceed fibrils, so-called roots of the cilia, which traverse the rest of the cell and converge like a cone toward its base. If the cilia become separated from the basal corpuscles they cease to beat; but if attached to their basal corpuscles the cilia of even a small fragment of a cell in a preparation of living tissue will show just as lively movements as occur in entire cells, or in an intact epithelium.

These protoplasmic threads, the cilia, are contractile and the stroke of the movement given by all the cilia of all the cells of the one epithelium is always in the one direction; so that the movement of a fluid resting upon the cilia also proceeds steadily in a constant direction. In the human body this movement is always toward the external openings of the body, in the respiratory tract toward the nasal openings and in the female genital tract toward the exterior. In such manner foreign bodies of not too great size are moved along with the ciliary stream; thus dust particles, and especially very fine particles of carbon, are removed from the respiratory tubes by ciliary action.

Ciliary movement is an entirely automatic type of movement which continues at the same speed without pause and without control on the part of the nervous system. In contrast to amœboid movement (p. 18) no stimulus as exciting cause is necessary; nor are there pauses in the motion. It is indepedent of the remaining processes of life to such an extent that not only can it be studied for hours in living tissues removed from the body of cold-blooded animals, but it can even be observed in very small fragments of cells. Such fragments commonly rotate upon their own axis as a recoil from the stroke of the cilia. After death, even death of the human body, ciliary movement continues for hours. In comparison with amœboid movement, which is always slow, the movement of cilia is relatively rapid.[1]

In many lower animals in addition to ciliated cells there are flagellate cells; *i. e.* cells with a single contractile hair which usually attains a considerable length and is stouter than a cilium. This flagellum also is rooted in the centrosome of the cell. In man and the higher animals only the male sex-cells, the spermatozoa, or better the sperms, are flagellate cells.

Ciliated epithelium is much more widespread in the embryonic condition than in the adult body; it is replaced by other types of epithelium during development, consequently in the adult body cilia may be found in unaccustomed places (as variations).

In contrast to the free surface of the cell with its numerous differentiations, the basal and lateral surfaces of epithelial cells are devoid of membranes. The lateral surfaces, and in stratified epithelia the basal surfaces as well, are usually connected by cement to those of the neighboring cells, or in the case of simple epithelia they rest on the basal membrane; more rarely the connection occurs by means of intercellular bridges. In only a single exceptional case do epithelial cells form a network and become connected by continuity. Pl.39, Fig.6 This is the case of the so-called enamel pulp of the enamel organ of tooth development where abundant gelatinous intercellular substance fills in between the cells.

Considering next the structures within epithelial cells, several kinds of cytoplasmic differentiations appear; some of which occur in other cells, while the remainder are characteristic of epithelial tissue. Thus the internal reticular apparatus is demonstrable in most epithelial cells; gland cells in particular rarely fail to show it. Usually it lies above the nucleus and near the free surface of the cell; *e. g.* in columnar cells. It is not greatly developed but appears smaller than in many nerve cells. Usually it occupies a relatively small part of the cell and consists of a few closely intertwined threads (p. 5). In addition the cytoplasm of many epithelial cells contains pigment granules; these are partly of simple melanin pigment as in the cells of the epidermis, and partly of fuscin pigment as in the cells of the pigmentary epithelium of the retina (p. 16). Fibrillar differentiations are present in many epithelial cells; of these the most noteworthy are the so-called tonofibrils Pl.4, Fig.6

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[1] In considering ciliary movement in living tissues, *e. g.* epithelium from the oral mucous membrane of a frog, it must be taken into account that the speed of the movement as it appears under the microscope is due to the use of a necessarily high magnification. The microscope affects time and space.

of the epidermal cells which run as supporting fibrils from cell to cell, passing through the intercellular bridges.

Of quite another nature are many structures of threadlike appearance, commonly known as basal filaments because they give to the basal part of the cell an appearance of
Pl.3, Fig.9 being marked by parallel lines. Examples are the glandular cells of the pancreas and the
Pl.4, Fig.4 epithelium of the convoluted tubules of the kidney. Probably they are of the nature of
Pl.53, Fig.6 plastosomes, especially so since in related cells, (epithelium of the secretory ducts of many
Pl.61, Fig.3 salivary glands) the filaments easily break up into rows of granules. According to one idea, which however has little probability, these structures stand in relation to the secretion granules.

But cell inclusions of still other kinds are found in epithelial cells; *e. g.* fat, which occurs not only as lipoids but also as neutral fat, as in cells of the liver where in larger or smaller drops it even verges on the pathological. Peculiar granular inclusions are shown by many layers of cells in the stratified squamous epithelium of the epidermis and are
Pl.88, Fig.4 distinguished by their strong affinity for stains. This material, which often appears as
Pl.90, Fig.4 droplets or particles of irregular form is termed KERATOHYALIN; since like the nucleus it stains with basic dyes, it is believed to have a nuclear origin. The trichohyalin granules of the inner rootsheath of the hair are similar structures, only they stain with acid dyes. These granules bear the name of keratohyalin because it was assumed that they represent an antecedent of the true corneous material or keratin; but this assumption is erroneous since the granules are lacking in the very places where cornification is most dense, as in the nails. Keratohyalin and trichohyalin are not lipoid materials, and show no reaction toward the reagents used for staining fats. On the other hand ELEIDIN a similar material occurring also in many epidermal cells, does seem to be a lipoid but as a rule does not occur in a granular form but as a diffuse solution throughout the cell. Epithelial cells may become cornified, during which process they die as the cytoplasm is transformed into the typical corneous material and the nucleus disappears. Thus all the hornlike material of the bodies of men and animals consists of dead, cornified remains of former epithelial cells. The cornification of a cell probably does not involve the transformation of the entire cytoplasm into horn, rather it becomes dried out from loss of water at an early stage of the process. The formation of keratin proceeds from the fiberlike structures of the cortical layer of the cell, which although at first of protoplasmic nature, by gradual cornification are converted into keratin. The central part of the cell contains the remnant of uncornified cytoplasm and the nucleus; and after the complete destruction of the latter its former location still remains demonstrable as a cavity within the cornified body of the cell. The more the cortical layer of the former cell becomes changed into horn, the higher the degree of cornification.

Secretion in Epithelial Cells

One of the most important functions of epithelial tissue is that of SECRETION; it is also one that can be recognized morphologically, especially in the cells of glands. Although the secretions of the body are mostly produced in organs, the glands, constructed specially for the purpose, yet the ability to secrete is by no means lacking in many cells of surface epithelia. Secretion is an activity of the cytoplasm; everything about the process that can be morphologically recognized appears to occur in the cytoplasm, although without doubt the nucleus also plays a part. The process of secretion is one of the phenomena of the life of a cell and one which makes considerable demands upon the cell. The demands may be so heavy that the cell dies as a result, a victim of the process. Of the numberless cells which are continually dying in our bodies many, indeed the majority, die as a result of their activity in secretion. A secretion so formed as to involve the death of the cell is termed HOLOCRINE. If on the other hand the life of the cell is not menaced either as a whole or in part by the process of secretion and the cell discharges its secretion without dying, it is spoken of as a MEROCRINE secretion. If the latter type of secretion occurs without any great injury to the constituents of the cell, the term ECCRINE is applied to the secretion. Between the two extreme types, eccrine and holocrine there stands the APOCRINE. In this type a part of the cell is destroyed in forming the secretion, but only a part; the basal portion containing the nucleus remains and from it the cell is regenerated after the discharge of the secretion and before a new phase of secretion begins. The apocrine type of secretion is thus merocrine as well.

Pl.4, Fig.3
Pl.49, Fig.4

A holocrine type of secretion is shown by the so-called goblet cells and also by the cells of the sebaceous glands of the skin; most other glands have merocrine secretion, indeed the great majority of them are eccrine. The apocrine type of secretion occurs in many of the sweat glands of the skin, the mammary gland and other related glands.

Pl.4, Fig.3
Pl.49, Fig.4

The GOBLET CELL is at once a typical example of holocrine secretion and of the formation of secretion in a surface epithelium; for such cells are engaged individually in secreting mucus, and at the same time are scattered here and there between the non-secreting cells. They are especially to be found in the ciliated epithelium of the respiratory passages and in the intestinal epithelium, which is a simple columnar epithelium with cuticular border. In the latter example various stages of the formation of mucus are seen in the superficial zone of certain cells whose cuticular border is lost early in the process. In this manner of secreting mucus, the cell imbibes water so that the mucus-containing part swells up greatly, while the basal part of the cell, which does not share in the mucus secretion, shrinks, probably from loss of water on the part of its cytoplasm. This basal part of the cell contains the nucleus which has already become pycnotic, an indication of the approaching death of the cell.

When the formation of the mucus is completed the goblet cell has the form of a goblet without a foot. The cup is filled with the swollen mucus; the greater part of the cytoplasm forms a kind of shell, the so-called theca, around the mass of secretion which eventually escapes through a clearly defined, round opening at the top of the theca. The stem of the goblet is represented by the basal part of the cell containing the pycnotic nucleus. Gradually the secretion all flows out through the opening at the surface, the theca collapses and nothing is left of the former cell and its cuticular border save a slender dark-staining remnant, the nucleus of which has completely disappeared. It remains wedged in between the non-secreting columnar cells and slowly disintegrates.

Pl.3, Figs.10–12
Pl.51, Fig.4

The **secretions**[1] formed by glands or surface epithelia are almost without exception of a fluid nature; only the sex glands yield a cellular secretion. In most cases more than 90% of the secretion consists of water, (mucus, serous secretions, urine etc.); very rarely do lipoids determine the character of the secreted material. In spite of this even the most watery secretions do not appear as such within the cytoplasm, but as granular, non-fluid antecedents, the so-called **secretion granules**; by the gradual liquefaction of which the non-granular, fluid secretion is formed. At present it is the general opinion that the secre-

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[1] Those secretions which are injurious to the body and which as a result must be removed from it usually are called EXCRETIONS.

tion granules are formed indirectly through plastosomes (mitochondria), which first break up into fine granules, then fuse together again, so producing a secretion granule (p. 5) Before commencing to secrete, gland cells are rich in plastosomes the number of which diminishes as the formation of the secretion proceeds. The granules are small structures
Pl.3, Figs.10, 12 lying in the cytoplasm; they vary from one to a few μ in diameter and may be irregular
Pl.44, Fig.4 in form, though usually they are approximately spherical. Usually they are easily distin-
Pl.53, Fig.6 guished from the surrounding cytoplasm by staining more strongly with many dyes, espe-
Pl.54, Fig.6 cially those of acid reaction; they show selective staining, but naturally just which stain will best demonstrate them depends upon the chemical properties of the secretion. The granular antecedents of mucus are especially sensitive to water, so that they never appear in goblet cells if the preparations pass through aqueous solutions.

But if the latter are avoided granular antecedents of the mucus secretion will appear, just as they appear in the preparation of other secretions. Premucin granules are thus demonstrable not only in goblet cells, but in the mucous portions of the salivary glands, and elsewhere sporadically in surface epithelia where the formation of mucus is occurring; *e. g.* in cells of the simple ciliated epithelium of the oviduct. True goblet cells are absent
Pl.3, Fig.11 from this epithelium, and the process of secretion does not end in the death of the cell. But elsewhere there are glands in which the demonstration of secretion granules, which may well be termed zymogen granules, is easily successful and other glands in which it is accomplished with difficulty. Frequently the ease of demonstration is connected with the chemical constitution of the secretion. For instance where this is of a lipoid nature, as
Pl.92, Figs.8, 11 in the sebaceous glands of the skin, it is easy to follow the formation of the secretion granules, their growth and the complete utilization of the cytoplasm in the formation of the lipoid granules; all because of the different chemical constitution of the cytoplasm on the one hand and of the secreted material, or its antecedents, on the other. The secretion of the fatty materials of the milk in the mammary gland is a similar case.

When the granules of a secretion antecedent appear in the cytoplasm of a cell, either
Pl.3, Figs.10, 12 they are present everywhere in an even distribution throughout the cytosome or their presence is restricted to a definite portion of the latter. Thus in many gland cells it appears that the formation of secretion granules occurs only in that zone of the cell which is turned toward the lumen, and that the basal part of the cell forms no secretion granules. When the formation of secretion granules is completed in the superficial part of the cell — that next to the lumen — then their liquefaction begins in the same part, which is accordingly named the general secretion zone. The discharge of the secretion then follows. Liquefaction of the granules is preceded by a gradual diminution in their ability to take a stain, so that the completion of the formation of secretion within the cell is recognized by the lessened ability of the granules to stain. Along with the formation of secretion there usually goes a noteworthy increase in the volume of the cell; and with the discharge of the secretion a corresponding diminution in volume.

The localization of secretion to a restricted portion of the cell and the phenomenon of the formation of a general secretion zone occurs only in merocrine secretion. This is especially the case in the apocrine type in which the whole general secretion zone of the cell is abstricted as a lobe of the cytosome after the formation of the secretion is completed. There are also cases of the eccrine type in which the formation of secretion embraces the
Pl.47, Figs.4, 5 entire area of the cell as in the parietal cells of the gastric glands.

The condition just mentioned is the rule in holocrine secretion. Thus in the secretion of sebum the lipoid secretion granules appear throughout the whole extent of the cytosome,

while the quantity of cytoplasm is correspondingly diminished; until at last there appears in the cell a typical honey-comb structure, the alveoli of which are more or less spherical and grow rapidly with the advance in the formation of the secretion. The secretion granules Pl.92, Fig.8
lie in the alveoli and the walls of the honey-comb are formed of the cytoplasm. The further secretion advances the thinner do the walls become, until finally the last remnants of them are used up in forming secretion. Since the nucleus has meanwhile disappeared by pycnosis, the former cell has become a spherical mass of liquified secretion granules and constitutes the glandular secretion, the former cellular nature of which is no longer apparent.

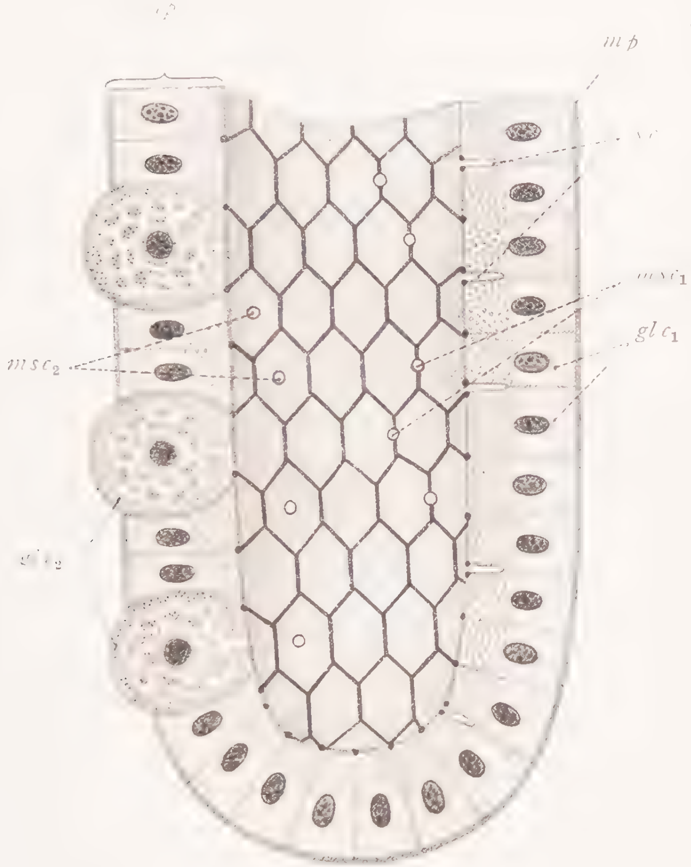

Fig. 7. **Diagram of a Gland with Intercellular and Intracellular Secretion Canaliculi.**

Part of a tubular gland divided longitudinally. To the right and beneath only columnar cells are represented in the wall. Toward their free ends secretion granules are visible on the cut surface; while intercellular secretion canaliculi lie between. Among the columnar cells to the left are to be seen large spherical cells which are quite filled with secretion granules and show intracellular secretion canaliculi. In the middle of the figure part of the lumen and some of the inner surface of the wall are shown with the network of terminal bars and the openings of secretion canaliculi.

$gl\,c_1$ = columnar cells of wall of gland
$gl\,c_2$ = large, spherical cells with intracellular secretion canaliculi
ep = epithelial wall of gland
$m\,s\,c_1$ = mouths of intercellular secretion canaliculi
$m\,s\,c_2$ = mouths of intracellular secretion canaliculi
$m\,p$ = membrana propria
$s\,c$ = intercellular secretion canaliculi

The secretion is not always discharged into the lumen of the gland, or upon a free surface, in such simple form as in this case of holocrine secretion. Often there are special Fig.-
passages conducting the secretion into the true lumen; these are termed SECRETION CA- Pl.4, Figs.10,11
NALICULI, or less aptly secretion capillaries. This type of adaptation is not found in all Pl.44, Fig.4
glands; in holocrine as well as in apocrine secretion such a device is superfluous, neither is it always to be found in eccrine secretion. The canaliculi are always fine tubules, without Pl.52 Figs.3,4
walls of their own, which either lie within the body of the cell, intracellular secretion canaliculi, or occur between cells and are then termed intercellular secretion canaliculi. In the latter case a canaliculus is formed by matched grooves in the opposed surfaces of neighboring cells. This type is observed in cases where the cells form a general secretion

zone; and the canaliculus extends from the central lumen between the neighbouring cells, but only in the region of the secretion zone and not to the base of the cells.[1] Intercellular secretion canaliculi are thus usually short fine tubules with blind ends. Intracellular secretion capillaries occur in glands of the eccrine type of secretion where the cells have no general secretion zone but form secretion in all portions of the cytosome. In such cells, *e. g.* the parietal cells of the gastric glands, the removal of secretion from the part of the cell distant from the lumen would be almost impossible without the special device of intracellular secretion canaliculi. In such cases the whole cytosome is traversed by a system of net-like anastomosing canaliculi which finally open into the lumen of the gland by a pore lying on the surface of the cell. The network of canaliculi is able to collect secretion from all parts of the cell, even those most distant from the lumen.

Between these two types of secretion canaliculi, the intercellular as found in the serous salivary glands, and the intracellular as found in the parietal cells of the stomach, there Pl.52, Figs.3,4 stand midway the secretion canaliculi of the liver, which have long been known under the name of bile capillaries. They lie between the liver cells in true intracellular fashion and form anastomosing networks which correspond to the peculiar netlike structure of the liver (q. v.). From them short, intracellular processes extend into the liver cells themselves and end there blindly. Probably these processes are of a temporary nature, forming as needed and again disappearing; for it is, on the whole, a question whether secretion canaliculi are permanent structures or are formed just as needed.

So far the discussion of the phenomena of secretion in epithelial cells has had reference only to the cytoplasm, not to the nucleus. Without doubt the process of secretion in a cell, representing as it does one of the three life processes of cells which may be demonstrated morphologically, is primarily a function of the cytoplasm. The view has also been expressed that in this function the nucleus plays an active role, giving origin to the secretion granules which thus must be considered almost as chromidia (p. 5). But this is hardly probable; although doubtless the process of secretion is regulated by the nucleus. Thus in the nuclei of secreting cells there are often to be recognized very clearly certain signs of activity not seen in the nuclei of non-secreting tissues; in this case the habitus of the nucleus in many ways recalls that of the beginning of mitosis.

Glands

By the term gland there is understood an organ which yields a definite secretion; *e. g.* the salivary glands yield saliva, the sweat glands yield sweat. Glands consist of epithelial tissue, at least as far as secretion is concerned this tissue alone enters into the question; but almost every gland includes a greater or less amount, usually quite small, of connective tissue which carries the blood vessels necessary for the nourishment of the glandular epithelium. This connective tissue of the gland, particularly in large glandular organs, is termed interstitial tissue, or STROMA, while the secreting substance of the gland bears the name of PARENCHYMA.

There are two types of glands corresponding to two different modes of transporting the secretion, those with external secretion or exocrine glands and those with internal secretion or endocrine glands. The first are officially termed *glandulae evehentes*, the latter *glandulae clausae*. The exocrine glands empty their secretion upon the free surface of the skin or into the interior of a hollow organ (intestine, respiratory passage, cavities of the genito-urinary organs) either directly, as in simple glands, or with the aid of a system of ducts as in compound glands. On the other hand the endocrine glands transfer their secretion to the blood stream; they thus have no ducts and are termed ductless glands. While the product yielded by exocrine glands is termed an external secretion, that of endocrine glands is known as an internal secretion. Since the latter is distributed by the blood stream throughout the entire body it acts not merely at, or near, the place where it was formed but also at a distance; internal secretions are hence termed hormones. There are glands which have both internal and external secretions.

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[1] If terminal bars are present, the mouth of the short intercellular canaliculus lies in the bar itself.

The glands of external secretion are the more numerous. To them belong the glands of the skin (sweat glands, sebaceous glands, mammary gland), the glands of the digestive tract (small glands of the mouth cavity and the large salivary glands, small mucous glands of the pharynx and oesophagus, glands of the gastric wall and those of the intestine, liver, pancreas), and the kidneys; also the reproductive glands, both chief glands (testis or ovary) and accessory glands (prostate, seminal vesicles, bulbo-urethral glands in the male; uterine glands, vestibular glands in the female), the lachrymal glands and those of the eyelids; also in a certain sense the lungs.

The glands of internal secretion are the thyreoid, the adrenals, the parathyreoids, the hypophysis (but only the anterior lobe),[1] the pineal body, the carotid glands, and a portion of the pancreas (the islands of Langerhans). The position of the thymus body is doubtful. But the spleen, the lymph glands, the tonsils and the interstitial cells of the testis and ovary[2] do NOT belong to the glands of internal secretion; nor indeed among the glands at all.

Endocrine Glands

Endocrine glands are more simple in structure than are exocrine glands. According to their structure two subdivisions may be made, the essential difference being that many glands of internal secretion are at first like exocrine glands, and only become endocrine glands secondarily from the loss of their ducts during development. A typical example is the thyreoid gland, the prototype of one variety of the glands of internal secretion. Although the structure of the gland is everywhere absolutely the same, for even the remnants of the ducts which often escape complete degeneration show the same structure as does the rest of the gland, yet the presence of cavities surrounded by the glandular cells is a sign that the organ originally began as an exocrine gland. In these cavities the secretion collects before it enters the blood stream. Such vesicles filled with secretion are called follicles Pl.59, Figs.4, 5 and the contained secretion is given the very inappropriate name of "colloid". Except Pl.60, Fig.1 in the thyreoid gland this condition, and consequently this type of endocrine gland, Pl.31, Fig.4 is found only in a part of the hypophysis; elsewhere follicles filled with colloid occur only occasionally and in quite rudimentary form.

The second structural type among endocrine glands, the so-called epithelial corpuscle type, contains no cavities filled with colloid. All these glands consist of masses or strands of epithelial cells in which often no definite manner of arrangement is demonstrable. Pl.76 Connective tissue, bearing blood vessels, separates the groups of epithelial cells. With the exception of the adrenal bodies all glands of this type are quite small and many of them, such as the carotid gland, have no sharply marked boundaries but fall into separate parts. The adrenals, more than all the other glands of this type show a great regularity of structure, but according to both structure and function consist of two separate parts which in lower vertebrates are two entirely distinct glands. To this category of endocrine glands, in addition to the adrenals, there belong the greater part of the glandular substance of the hypophysis, the pineal body, the parathyreoids, the carotid gland, and the islands of Langerhans in the pancreas.

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[1] Some investigators have prepared extracts of the posterior lobe which seem to contain a hormone. Trans. Note.

[2] Much evidence has been brought forward that the interstitial cells prepare a hormone; for those of the testis the case is particularly strong. — Trans. Note.

Exocrine Glands

The simplest form of exocrine gland, which however is of rare occurrence in man, is the so called ENDO-EPITHELIAL gland; *i. e.*, an indentation occurring in the thickness of an epithelial layer and lined by secreting epithelium. Glands of this kind are naturally very small; in man they are found only in the wall of the efferent ductules of the epididymis.

Pl.66, Fig.7

All other forms of exocrine glands are so-called EXO-EPITHELIAL glands; *i. e.* the secreting gland proper, along with its duct, lies outside of the epithelial layer upon which it empties, and is situated in the subepithelial connective tissue. Thus the glands of the skin are situated in the corium, and those of mucous membranes lie within the tunica propria. As a rule a gland is separated from the surrounding connective tissue by a basal membrane (membrana propria) of connective tissue origin. Different subdividions of such exo-epithelial glands have long been made on the basis of the geometrical form of the gland or rather of its terminal secreting parts. If the gland, or its secreting parts, are spherical saccules it is spoken of as an ALVEOLAR gland; if they are tubelike it is called a TUBULAR gland. While in simple glands only these two fundamental forms are realized, in the large, compound glands intermediate forms predominate to which the name TUBULO-ALVEOLAR has been given. In this case the basic form of the terminal part is tubular, though often very short; but upon the tubule are situated spheroidal appendages. At times the tubular character predominates, and at times distinct transitions to a purely alveolar type are found (alveolo-tubular). This classification of glands is very schematic, practically its utility is limited; the more so since undoubted individual variations in form occur. Moreover distinction must be made between the form of the whole terminal part (basal membrane + epithelium) and that of the lumen, which in size and form does not always correspond to the exterior. Simple and compound glands may be distinguished; all of the large glandular organs are of the compound type. In order to discharge the secretion from the entire gland through one duct the latter is branched, for only by branches can it enter into connection with the terminal secreting parts. According to the number of secreting parts the branching of the main duct must be more or less profuse; consequently in very large glands there is of necessity a very extensive DUCT SYSTEM. Considerable differences in structure may be recognized in the walls of the separate parts of this system of ducts. The branching of the duct system usually is such that the main duct gives off a relatively small number of quite stout branches, these in turn divide into branches of correspondingly lessened diameter, and this process is repeated many times; the branching thus resembles that of a linden or of a fruit tree; *e. g.* the salivary glands, liver, and lungs. In other cases, as in the pancreas, the gland is traversed axially by a main duct which increases in diameter toward its point of discharge and receives in its course relativly small branches of uniform caliber; this type of branching resembles that of a cedar or of a poplar tree. Frequently, as in many salivary glands and in the pancreas, there is interposed

Pl.41, Fig.3
Pl.42, Figs.1–3
Pl.43, Figs.2,3
and many other Figures

between the terminal secreting part and the end branches of the duct system proper a number of uniformly thin-walled connecting pieces of fine caliber which are branched to only a moderate degree; these are the so-called intercalated or intermediate ducts.

As may be imagined, when the gland is smaller the branching of the duct is less abundant; in quite small glands the duct is composed of very few branches. The relations are most simple in the so-called simple; *i. e.* not compound, glands. This is seen in many tubular glands; *e. g.* sweat glands of the skin, glands of the intestinal wall, uterine glands. Here in the simplest case the one tubule represents both gland and duct (where possible it is short and straight as well); or else a separate duct portion is not to be distinguished at all. Still there are glands of this simple form in which one part of the tubule has a secretory function, and another part serves as duct, for instance the sweat glands of the skin. If the tubule is forked at its base, and particularly if this process goes on to a considerable extent, then the simple tubular glands pass insensibly into compound glands having a duct system, although a very simple one. Alveolar glands consisting of but one al- Fig.8 veolus do not occur in man, but the sebaceous glands of the skin comprise very few (2—4) alveoli; commonly these discharge without a true duct.

Small glands, not merely the simple tubular glands but also the smaller forms of glands with duct systems, have their site quite within the mucous membranes or within the cutis of the skin. The ducts, which as far as they are present at all are quite short, penetrate merely the epithelial layer; in the case of the skin they penetrate the epidermis. Larger glands, especially the quite large glandular organs, lie at some distance from their point of discharge, so that the duct after leaving the gland often has a considerable length.

According to the possibilities mentioned above there are six different types of glands in the human body, though not all of them are realized in clear-cut form.

1. SIMPLE TUBULAR GLANDS. These may either have the form of simple unbranched tubules, or they may be branched. The simple unbranched tubular glands occur as short straight tubules (Lieberkühn's glands of the intestine) or as long tubules with the terminal part coiled into a knot (sweat glands of the skin, wax-secreting glands of the external auditory passage, Moll's glands in the eyelids, and some others). In the sweat glands only the coiled, blind end of the tube serves as a secreting portion; the straight part of the tube represents the duct. To the simple branched tubular glands belong most of the fundus glands of the stomach and the uterine glands.

2. COMPOUND TUBULAR GLANDS. These consist, so to speak, of a complex of simple branched glands which discharge through one common duct. The terminal tubules are for the most part short, as in the simple branched glands. In some glands, *e. g.* the testis, there are anastomotic connections between the terminal tubules, a transition to the reticular type of gland. In addition to the testis the kidneys, the lachrymal glands, and the serous glands of the tongue are compound tubular glands.

3. SIMPLE TUBULO-ALVEOLAR GLANDS. These occur only in the branched form as the pyloric glands of the stomach, Littré's glands of the urethra (glandulae urethrales) and the small mucous glands of the upper part of the digestive tract.

4. COMPOUND TUBULO-ALVEOLAR GLANDS. These consist of a complex of similarly formed, simple glands connected to a common duct system. This is the most frequent type of compound gland. Here belong the large salivary glands, the sublingual gland being quite typically tubulo-alveolar; while the submaxillary gland is chiefly tubular in the mucous part and alveolar in the serous portion. The parotid gland has so far lost its tubular character as almot to deserve being termed a purely alveolar gland. To the

compound tubulo-alveolar glands belong also the pancreas, the prostate, the lungs, all the larger mucous glands of the respiratory and digestive tracts, the duodenal glands, the bulbo-urethral glands and the mammary gland.

5. SIMPLE ALVEOLAR GLANDS. These occur in unbranched form and without true ducts as in the small sebaceous glands; or they are branched and have real ducts as in the large sebaceous glands and in the glandulae tarsales or Meibomian glands.

6. COMPOUND ALVEOLAR GLANDS. This form is very rare and occurs as a transitional type (alveolo-tubular) and only in the parotid gland. Even in this gland observations do not all agree; if it is considered to be tubulo-alveolar then there are no compound alveolar glands in the human body. This view is more likely to be correct than to consider it purely alveolar, although it does nearly approach the latter form.

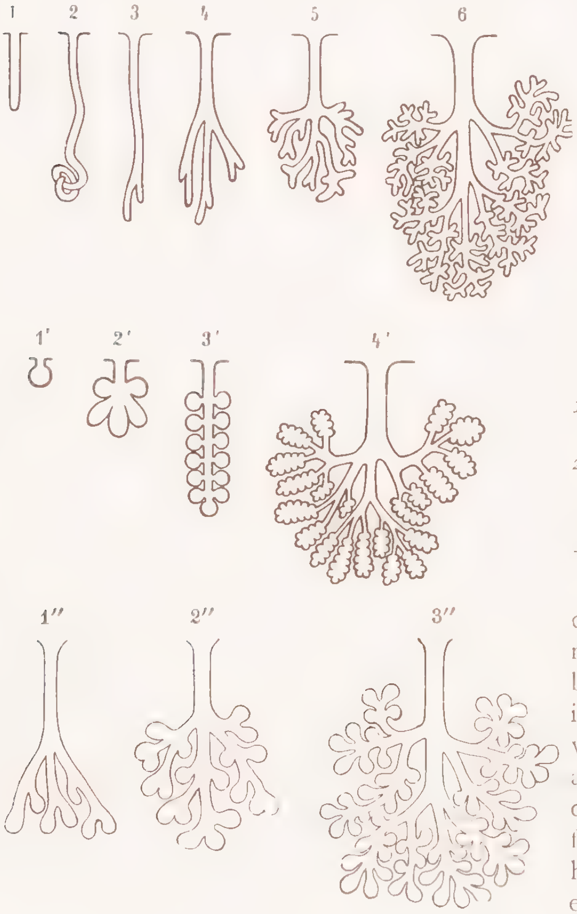

Fig. 8. **Diagram of the Types of Glands Found in Man.**

1 = simple tubular gland, straight and unbranched
2 = simple tubular gland with coiled end
3 = simple tubular gland with bifurcated end
4 = simple tubular gland with several bifurcations
5 = simple tubular gland with numerous bifurcations and duct system
6 = compound tubular gland
1' = simple alveolar gland of but one alveolus
2' = simple gland of several alveoli and duct
3' = simple gland of many alveoli and duct
4' = compound alveolar gland
1'' = simple tubulo-alveolar gland with several bifurcations
2'' = simple tubulo-alveolar gland with numerous bifurcations
3'' = compound tubulo-alveolar gland

Not all the glands of the human body can be fitted into this classification. Certainly not the liver which is indeed an exocrine gland but has an epithelium which is not formed into terminal secreting parts but into a network of connected cellular cords; thus there are no lumina in the liver surrounded by gland cells. In place of the missing lumina their function of receiving the secretion is taken by highly developed secretion canaliculi, which empty directly into the beginnings of the duct system, not into lumina. The comparative anatomy of the liver of the lower vertebrates shows that the liver as just described is to be regarded as a compound tubular gland, the tubules of which lose their lumina and anastomose forming a network. In a certain sense the liver may be termed a reticular gland.

The reproductive glands are further exceptions, especially the female gland. In the first place they differ from all other glands in not yielding a fluid secretion formed by epithelial cells in the manner described above for secretions; but their secretion is cellular. The cells which they secrete are the transformed daughter cells of the epithelial walls of their secreting parts. In the female reproductive gland the latter disintegrate early in development; while in the male the testis presents the picture of a true exocrine gland (p. 47) with a duct system. The female reproductive gland, the ovary, would at first appear to be an endocrine gland for there is no duct system in direct connection with it; yet it discharges its cellular secretion externally. To accomplish this the superficial layer of the organ, having previously become very thin, bursts open *(glandula dehiscens)*; however the ovary has no proper secreting parts such as are present in typical form in the testis.

In this discussion it has been assumed that usually a gland may be separated into terminal secreting parts on the one hand and into a system of ducts on the other. That is true for the great majority of glands; but there are beyond doubt cases in which secretion is formed in the ducts; *e. g.* in the ductus epididymidis, which is the upper part of the lengthy duct of the testis. The efferent ductules of the testis even have endo-epithelial glands (p. 48) and the ampulla of the ductus deferens, and its blind appendage, the seminal vesicle, secrete as truly as does a gland.

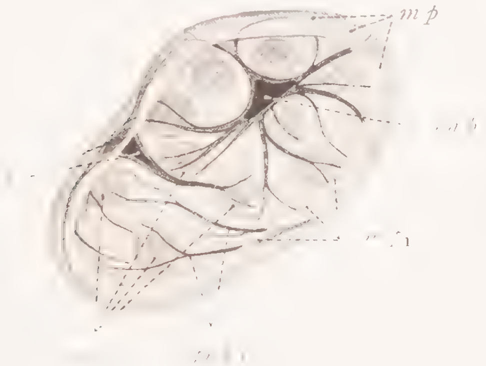

Fig. 9. **Diagrammatic Representation of Basket Cells.**

The diagram represents the terminal secreting part of a salivary gland. A large opening has been made in the membrana propria to display the basket cells, two of which are shown with parts of a third. Where it has not been removed parts of the basket cells are seen through the basal membrane. Beneath the basket cells are seen the glandular cells.

pr b c = processes of basket cells
nn = nuclei of glandular cells
nn b = nuclei of basket cells
m p = membrana propria seen from the surface
$m\,p_1$ = cut edge of membrana propria

The terminal secreting parts of the exocrine glands are formed of at least two chief consituents; the secreting epithelium and a basal membrane, or membrana propria. The latter separates the epithelium from the surrounding connective tissue and is itself of connective tissue nature; details on this point will be given later. But there are glands in which cells are placed between the epithelium and the membrana propria. Such cells are always flat, have a highly branched form and are placed at considerable intervals apart. They bear the name of **basket cells** because with their anastomosing branches they surround the epithelium like a basket. Probably these are myo-epithelial cells (p. 38), contractile elements such as are present in well marked form in the coils of the sweat glands where they assume the shape of the true, mesenchymatous, smooth muscle cells. The epithelial origin of such myo-epithelial cells is shown by their position inside the basal membrane; also in the sweat glands where the secreting part passes into the duct the gradual transition from smooth muscle cell to true epithelial cell can be shown. Basket cells are found especially in the salivary glands and in the mammary gland. Typical myofibrils may be demonstrated in them just as in true smooth muscle cells.

While the blood vessels of glands lie entirely within the interstitial connective tissue, the finest branches of the nerves (secretory nerves) pass through the basal membrane to the epithelial cells; at least this has been demonstrated beyond a doubt in many glands.

For the special features of individual glands see the chapters on the microscopic anatomy of the organs.

Supporting or Connective Tissue

To understand this tissue in its many forms, which in the fully developed body fall into subdivisions of highly varied character, it is necessary to take a glance at their embryonic origin. For no matter how widely different the separate subdivisions of connective tissue may appear, yet one and all are derived from the same primitive embryonic basis, the embryonic connective tissue or **mesenchyme.**

Mesenchyme is exclusively a formation of the middle germ layer; true connective tissue is consequently always of mesodermal origin.[1] On this point it stands in decided contrast to epithelial tissue which may be derived from any one the three germ layers (p. 32) and generally proceeds immediately from their epithelium-like lamellae. Such direct origin is out of the question with connective tissue. Rather the embryonic source from which connective tissue is formed is itself a secondary differentiation, but of the middle germ layer alone. From mesenchyme there is formed not only connective tissue but also muscular tissue, both true smooth muscle and probably a certain amount of striated muscle; but this fact is without great effect on connective tissue.

Mesenchyme is distinguished even in the first stages of its existence from the epithelial lamellae of the germ-layers. That which throughout life holds good for almost all the cellular elements of connective tissues, holds also for the cells of the embryonic mesenchyme; they are branched cells, connected by continuity, and form nets (p. 31). All these cells are derived from the middle germ layer; one by one in definite localities they move out of the epithelial-like formation in which the cells of the layer are arranged. At first they show amœboid movement, then through their processes they enter into connection with one another on all sides and thus form the primitive cell net of the embryonic mesenchyme.[2]

The parts of the middle germ layer where this manner of mesenchyme formation goes on, are, in the first place, the mesodermic somites from which are derived both the axial connective tissue (sclerotome) and that of the skin (dermatome); secondly the visceral lateral plate, from which come the parent cells of the embryonic connective tissue of the intestine, but without destroying the epithelium-like structure of the plate. By contrast the epithelium-like parts of the somite wall which give rise to connective tissue are entirely used up in forming mesenchyme. These cells fill the interval, previously empty, between the germ-layers.[3] As already mentioned beside the general connective tissue they give rise to the smooth muscle of the viscera and of the blood vessels, to the striated muscle of the heart and to many another striated musculature such as that of the tongue, pharynx and oesophagus, but this discussion is immediately concerned with connective tissue only.

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[1] The notochord and the so-called chordal tissue of which it consists consequently do not belong to connective tissue; for the notochord is formed from the inner germ layer, and in its histological structure is very different from connective tissue. Neither has it been proved that the connective-tissue chordal sheath is formed by the cells of the notochord. Rather there are highly probable findings according to which the tissue of the chordal sheath comes from the mesenchyme.

[2] In living embryos of the lower vertebrates the amœboid movement of the young mesenchyme cells is easily recognized under the microscope.

[3] Hence the name mesenchyme which signfies "that which is poured into the middle". That is to say, the mass of cells secondarily filling in between the epithelial lamellae of the germ layers.

As soon as the embryonic mesenchyme has filled with its chains of cells the intervals between the germ layers, a fluid may be recognized in the spaces between their anastomosing processes; this may be termed the primitive intercellular or ground substance. At first it is entirely free from secondary, fibrillar structural elements (p. 31). From the cell net of embryonic mesenchyme there proceed all the cellular elements of the connective tissue of the fully developed body, including the cells of the blood and the endothelium; and indirectly all the fibrillar elements of connective tissue as well, since they are formed either from the cells themselves, or at least through their agency.

Thus embryonic connective tissue at first consists only of a network of cells. But relatively early in embryonic life there appear fibrillar elements so that from the embryonic period onward connective tissue consists of its two main constituents, cells and fibers. Furthermore differentiations occur within the mesenchyme relatively early in embryonic development and indicate its subdivision into large tissue groups. In particular three great subdivisions of connective tissue can be distinguished even in the embryo, connective tissue proper, cartilage, and bone; and from special groups of mesenchyme cells there arise both the cells of the blood and the endothelial cells.

Disregarding the last named substances, which will be discussed after the tissues proper, in the following description of the connective tissue of the adult body two structural elements find place, cells and fibers. Since the greatest variety of differentiation in both of the elements of connective tissue occurs in connective tissue proper, this will be the first subdivision to be considered. Cells and fibers will then be familiar when met with in similar form in the other two subdivisions.

Connective tissue thus falls into three great subdivisions, 1. CONNECTIVE TISSUE proper, 2. CARTILAGE, 3. BONE.

Since all the cellular elements of connective tissue are allied to one another and also more or less directly the fibrous elements as well, the three chief subdivisions of connective tissue remain during life in close mutual relationship. This will best appear from their ability to replace one another; less often in one species of animals, but rather in the sense that one kind of tissue is used in the one species in a situation where another tissue is used in the other species; *e. g.* cartilage in place of bone.

1. Connective Tissue (Proper)

Connective tissue in the narrower sense is made up of cells and fibers. Considering first the cells it is seen that the cell nets of embryonic connective tissue are repeated in those of the adult body; not in an equally clear manner in all the varieties of connective tissue, but yet in a form which corresponds throughout to the mesenchymal mother tissue. The connective-tissue cells which thus form nets are named **fibrocytes** because the fibrous elements of connective tissue, even in the embryonic condition, were either formed from them directly, or at least owed their formation to the influence of these cells. Thus the embryonic mesenchyme cells pass gradually into the fibrocytes of the more or less fully developed connective tissue.

Pl.5, Figs.1,2 Pl.6, Fig.6 Pl.7, Fig.5 It is an essential characteristic of fibrocytes that in almost all places where they occur they form cell nets; a peculiarity which can be recognized in bone as well as in connective tissue. Only in cartilage are the fibrocytes not connected with one another by processes.[1] Since they have to do with the fibrous intercellular substance they are also well named fibroblasts; the term ordinary or fixed connective-tissue cells was in earlier use, and still earlier that of connective-tissue corpuscles. The appearances which these cells assume may vary considerably even in different varieties of connective tissue proper; because the situation of the cells in the fibrous intercellular substance, under certain conditions, is of considerable influence both upon the manner of their arrangement and upon their form. As a rule the cells are very flat; seen from the surface they show an irregularly polygonal outline which occasionally is elongated and frequently star-shaped. The short elliptical nucleus lies centrally in the cell; it also is flat and for that reason when seen from the surface appears very large. From the cell there extend processes which unite with those of neighboring cells; although they may be either broad or slender they are always flat like the cell itself and frequently are forked at the end. Viewed in profile the fibrocytes appear "spindle-shaped", often indeed almost like short lines; in which case the greatly flattened nucleus is especially apparent. The thickness of the cell at its maximum is scarcely more than 1 μ and the processes are still thinner; while the nucleus is so flattened as scarcely to cause the cell to bulge. Without its processes the cell covers an area of 20 μ and more. The cytoplasm is very delicate and, largely due to its extreme thinness, very transparent in the perfectly fresh condition; but with the aid of appropriate staining there may be recognized structures, such as plastosomes, melanin pigment (p. 15), fat in larger or smaller droplets (p. 68), and fibrillar structures which may be tonofibrils. The centrosome is demonstrable as a diplosome. The outline of the nucleus is usually even, but indented kidney-shaped nuclei do occur; the chromatin appears finely divided and scattered nucleoli are present. Now and then the branching of the fibrocytes is strikingly regular and at the same time very abundant as in the cornea of many animals; Pl.6, Fig.6 however this is much less marked in the human cornea. Fibers and bundles of fibers which run over the bodies of the fibrocytes frequently produce furrowlike impressions on the cytoplasm and even on the nucleus itself.

While many varieties of connective tissue, even those of connective tissue proper, contain only fibrocytes; other types of cells may occur, particularly in unformed, loose Pl.5, Fig.2 connective tissue. To these belong the **wandering cells** which are a part of the great category of colorless blood cells; by means of their amœboid movement (p. 18) they wander through the connective tissue. Since this type of cell will be treated in detail in the discussion of the cellular elements of the blood their description may be omitted here. They are cells which come from the blood and either have passed through the vessel walls in order to gain the connective tissue or are just reversing this process; or else they are the so-called histiogenic wandering cells which spend all their lives within connective tissue but wander about in it. The latter type of wandering cell occurs in widely varying numbers; most kinds of human connective tissue contain only a few but they are much more numerous in many mammals. Along with them occur still other cells of the great group of the colorless blood cells; namely the EOSINOPHILE LEUCOCYTES (The Blood, p. 89). In man they are found only in definite localities; viz. in the intestinal mucous membrane, the great omentum, interstitial tissue of the lungs and mammary gland. The eosinophilic cells of the intestinal mucous membrane are histiogenic cells whose eosinophilic granulations form in loco. This is in contrast to other such cells in connective tissue which come from the blood.

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[1] The original connections of the fibrocytes, which are uniformly lost as the cartilage forms from the mesenchyme, are also occasionally wholly or partly lost in other places, as in tendon cells.

The name of resting wandering cells, or better of **histiocytes** is given to certain connective tissue cells which in many ways may appear very similar to fibrocytes but differ considerably from them, especially in their origin. These cells have received other names, such as "adventitia cells" because often, if not always, they lie along the course of small blood vessels; or "clasmatocytes" because it was thought they could shed their granular processes which were supposed then to dissolve in the intercellular substance. Their designation as resting wandering cells has been given them because they are believed to be derived from amœboid wandering cells which, so to speak, have halted in the tissue to rest; and that under certain conditions, usually of strong stimulation, they may again become motile, wander about, act as phagocytes etc. The correctness of this view is generally admitted today in spite of the great external resemblance of the cells to fibrocytes, especially in man.

Pl.5, Figs.1,2
Pl.6, Fig.5
Pl.23, Fig.5

In spite of their great similarity of external form they are distinguished from fibrocytes in the first place by not forming cell nets. In places where they are situated relatively close together and put out processes, they nevertheless remain independent, and establish no connections with one another, their boundaries being sharply defined. In form they are now slightly rounded, now elongated and spindle-shaped with thickened clublike ends or even with branched processes, in which case they may be mistaken for fibrocytes. In man the elongated and branched forms are abundant. The nucleus is constantly smaller and less flat than that of a fibrocyte, and being also richer in chromatin it stains definitely darker; often it has an irregular contour or an elliptical or reniform shape. The cytoplasm of histiocytes stains more strongly than that of fibrocytes and in general the demarcation of the cell is much sharper. Frequently granules due to phagocytosis are found in the cells especially in the rounded processes. The centrosome is easily demonstrable as a diplosome. These cells are very distinctly recognizable through the peculiarity of showing very brightly stained granules when connective tissue is treated supravitally with solution of neutral red.

Supravital staining with neutral red succeeds especially well in the looser subcutaneous tissue of the rat and mouse, which in general is much richer in cells than that of man; and is especially rich in amœboid wandering cells and histiocytes. The latter are here more rounded in form and not elongated and branched as in man. Even under low magnification they are noticeable after the action of neutral red because of their intensive red color. In addition they are stained selectively by lithium carmine and certain acid aniline stains (trypan blue, isamine blue and pyrrhol blue), the use of which demonstrates granules of considerable size.

Granular foreign material which reaches the connective tissue is soon phagocytosed by the histiocytes, which in consequence may be termed fixed phagocytes in contrast to those which are amœboid. These cells are found in very different parts of the connective tissue, very abundantly for instance in the great omentum and mesenteries, and as mentioned before along the course of blood vessels, especially the small ones. In places their number is scarcely less than that of the fibrocytes, while in other places they are scarce.

Pl.23, Fig.5

While the genetic connection of the resting wandering cells with the related forms of colorless blood cells, particularly with the amœboid wandering cells, may be proved in the sense that the one type can pass into the other; the question whether resting wandering cells may eventually transform into fibrocytes is as yet undecided. Without doubt certain cells may be observed in connective tissue which can be claimed to be transition forms between the two types.

Thus both the amœboid and the resting wandering cells are to be accounted members of the great group of colorless blood cells and the same is true of the two remaining types of cells found in connective tissue; viz. plasma cells and mast cells. As regards **plasma cells** they are usually spherical elements; in any case, apart from the amœboid wandering cells which may also be spherical, they represent the only category of connective tissue cells, otherwise so flat, which approach a spherical form. However plasma cells are not always spherical; where they lie closely side by side in large masses, as is not infrequently the case, the spheres are distinctly flattened against one another, and where they lie in narrow spaces they are pressed correspondingly flat; neither have they always even contours. This might imply amœboid movement in this group of cells also; but it is a question whether these cells have such powers; in any event the latter cannot be very great. After all the basic form for plasma cells is the spherical — and in such form they are found in the majority of preparations. Pl.5, Figs.2,4

An essential characteristic of the plasma cells is the basophilic reaction of their cytoplasm, which may always be clearly recognized, even though naturally it is not nearly as intense as that of the nucleus. The staining affects the cytoplasm quite evenly; except that near the nucleus there remains unstained a more or less crescentic zone, the so-called juxtanuclear "vacuole". The nucleus of the plasma cell is small and spherical, usually it lies excentrically; exceptionally there may be two nuclei. The chromatin is subdivided into coarse masses placed on the inner surface of the nuclear membrane and along radial lines, though somewhat irregularly, hence the term "wheel" given to the nuclei of plasma cells.

The size of plasma cells may vary considerably, however in the majority of cases the variation is small and the cells rarely exceed 10 μ; but occasionally they become much larger, almost twice as large. The occurrence of the cells is quite variable. In the looser, unformed connective tissue, otherwise so rich in cells, they are very rare or are entirely lacking; on the other hand they occur among the numerous cells of the omental connective tissue, in the interstitial connective tissue of many glands and in the mucous membrane of the nose, intestine etc. Frequently they are arranged around small blood vessels; in some places they form compact masses while in others they occur singly.

It is now generally admitted that plasma cells are formed from large or small lymphocytes which, following alteration in their structure, settle in the connective tissue. Thus the lymphocytes of the blood, like the amœboid wandering cells of the connective tissue, enter into the discussion. This would mean that plasma cells are wandering cells of lymphoid nature but at rest like histiocytes; only their rest is permanent though short. It is thought that they are short-lived cells which soon disintegrate, for many of the phenomena of degeneration have been observed in them. This also explains why these cells are at times common and at other times, in the same place, are rare.

Mast cells, the last type of connective tissue cells to be discussed here, are primarily distinguished by containing basophilic granulations in their cytoplasm; indeed it is quite filled with them. The size of the granules varies even within the same cell. They are easily demonstrated by basic stains, especially aniline stains, or by haematoxylin; on the other hand they are rather indistinct in the fresh condition because of their slight refractive power. As regards their shape mast cells are flat, but by no means extremely so, and have a round or elliptical outline. In rare cases they have an elongated form or short, plump processes. The central, or approximately central, nucleus is spherical or of slightly ellipsoidal form; only rarely does it show indications of polymorphy, such as slight lobulation. Pl.5, Fig.5

Mast cells occur singly, in more or less limited groups, or very frequently close together in rows along the course of blood vessels. They are rarely to be found except in loose, unformed connective tissue and even here in variable number and arrangement. In mice and rats whose connective tissue is exceedingly rich in cells, mast cells are present in large numbers. Their granulations are soluble in water so that as a rule they are only to be observed in such preparations as have not passed through watery solutions, or through alcoholic solutions of less than 70% strength. Since basophilic granulation is the only certain mark which mast cells display, the results from preparations are not reliable unless the above mentioned precautions have been taken. Mast cells whose granulations have been dissolved may appear like plasma cells etc. The size of mast cells varies, it is true, but is usually greater than that of plasma cells. The variable number in which mast cells occur in similar places supports the view that they are not structures of long life but, like the plasma cells, soon die.[1]

It may be imagined that mast cells come from the blood and are thus basophile leucocytes which have wandered out of the blood stream (p. 89). However their haematogenous origin is vigorously disputed and it is asserted that they are of purely histogenous origin; *i. e.* histogenous mast cells, in contrast to the mast cells of the blood. (Concerning the difference see the chapter on the blood.)

We have thus become acquainted with the following types of connective-tissue cells: 1. Fibrocytes, the direct descendants of the cells of the embryonic mesenchyme, and as a result present in all varieties of connective tissue; 2. amœboid wandering cells; 3. eosinophilic cells (leucocytes); 4. histiocytes (wandering cells at rest); 5. plasma cells; 6. mast cells. If still another variety is now described, viz. **pigment cells**,[2] it is not at all a question of Pl.5, Fig.6
a special type of cell but, as it were, of a subvariety of the fibrocytes. As a rule these cells, Pl.70, Fig.1
by their content of pigment on the one hand and by the early, usually embryonic differenti- Pl.78, Fig.1
ation of the subvariety upon the other have attained a unique place. This is especially to be recognized in the lower vertebrates in which the pigmented connective-tissue cells, pigment cells or chromatophores as they are also called (p. 17), play a disproportionately greater rôle than in man.

As already mentioned connective-tissue pigment cells are rare in man, and consequently it is unusual to find pigmented connective tissue, or pigment tissue as connective tissue is called when the cells, more or less as a whole, contain pigment. This applies solely to melanin pigment,[3] which in the human body is not constantly found in any quantity worth mentioning except in the middle coat of the eyeball. In this situation the majority, but not all, of the fibrocytes contain melanin pigment granules varying from brownish yellow to a dark brown color according to the general degree of pigmentation of the individual Since the whole cytosome is filled with such granules the processes of the cell, and consequently the cell nets, stand out very clearly. The same is true of the pigmented connective tissue of the corium in which, except in blemishes, pigmented connective-tissue cells are rare in the non-pigmented races; but they do occur in places as in the eyelid, area of the nipple, genital and circumanal regions. In addition scattered, pigmented, connective-tissue cells may be found in the membranes of the central nervous system and in the connective-tissue coverings of the labyrinth.

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[1] In preparations there are frequently found fragments of mast cells such as lumps of protoplasm with basophilic granulation. But such cases are not those of the death of mast cells but of artefacts; mast cells are very easily injured.

[2] Fat cells will be treated under adipose tissue.

[3] Occasionally lipofuscin pigment may occur in connective-tissue cells; and under pathological conditions, pigment of haematogenous origin.

It may be shown, especially in the bodies of the lower vertebrates where pigmented connective tissue is so wide spread, that pigment cells can increase in numbers by division. Mitotic divisions of pigment cells are easily observed, for instance, in the richly pigmented wall of the body cavity of amphibian larvae. The increase in number of pigmented connective-tissue cells proceeds in such fashion as to render it probable that from the relatively early embryonic stage, when autochthonous pigment was first formed in the cells (p. 17), pigmented cells have arisen only by division of the pigmented mother cells already differentiated. Still the fibrocytes of the later stages of development retain the ability to form pigment in their cytoplasm.

The so-called INTERSTITIAL CELLS OF THE REPRODUCTIVE GLANDS form a special variety of connective-tissue cell, proportionately larger, richer in protoplasm and more like epithelium. These cells are found chiefly in the testis and are relatively rare in the human ovary. They have erroneously been taken by many for epithelial cells, forming a gland of internal secretion; a thing which quite definitely is not the case.[1] Since in groups and chains they lie along the small blood vessels of the testis they are perhaps to be considered as histiocytes which have the special function of storing reserve materials for the gland.

Over against the cellular constituents of connective tissue there stand the **fibrous constituents,** for in contrast to epithelial tissue which is formed only of cells, connective tissue as a whole consists OF CELLS AND OF **fibers**. In fully developed connective tissue these latter structures, one and all, are independent of the cells and lie between them. They thus form in this tissue a constituent of the intercellular substance, in the widest sense of the word. However the fibers by no means form the whole of the intercellular material; in addition to the fibers there can be shown an intercellular GROUND SUBSTANCE which is homogeneous and amorphous, and which occurs in highly variable quantities in the different types of connective tissue.

In connective tissue, and in supporting tissues in general three different types of fibrous elements may be distinguished with certainty: 1. collagenous connective-tissue fibers, for the sake of brevity known simply as connective-tissue fibers or fibrils; 2. elastic fibers; 3. reticulum fibers, also named precollagenous fibers. Perhaps there is still a fourth type — pre-elastic fibers (p. 62).

Pl.5, Fig.1-3
Pl.6, Fig.1-3

The **collagenous** fibers are fine, transparent, of uniform or approximately uniform thickness (0.5 μ), and are probably very long, for their ends can scarcely be determined. They are distinguished from the two other kinds of fibers by never occurring singly but almost without exception in bundles; or without making true bundles they may form cordlike masses lying parallel and close together in greater or less numbers and seemingly united by a kind of cement. In contrast to the uniform thickness of the fibers of which they consist, these connective-tissue bundles are of highly variable thickness, depending upon the number of fibers which enter into their composition. As a result some bundles are very slender, only a few μ thick; and others which have considerable thickness, 20 μ and more. Collagenous fibers never form networks and never branch; although the bundles which they form do show a netlike arrangement, the so-called areolar connective tissue (p. 64). The cords or bundles which compose such nets may branch, and according to their thickness consist of more or fewer collagenous fibers. The term "collagenous" refers to the fact that upon boiling, the fibers yield gelatine. They have a low refractive index and appear faint in the microscopic picture; only by reducing the light sufficiently can the striation of the bundles be seen in fresh preparations. For corresponding to their composition from a larger or smaller number of fibers, the bundles appear finely striated.

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[1] See footnote 2, p. 47.

The collagenous fiber is a structure whose resistance is but slight; alkalies such as caustic potash produce first a swelling of the fibers and then dissolve them completely; acids such as diluted acetic acid cause marked swelling so that the fiber disappears from view. This effect is not uniform but in the course of a swollen bundle, ringlike constrictions occur the nature of which is not wholly clear (p. 65). Strong inorganic acids (hydrochloric acid, nitric acid) do not produce this swelling but in diluted form they act like acetic acid. By careful neutralization of the acid the swelling may be reduced and the fibers which had become invisible reappear in the microscopic picture as the striation of the bundle. The fibers are neither elastic nor extensible; if the bundle which they form is not stretched the longitudinal striation appears wavy, and this is usually the case in microscopic preparations. The fibers are doubly refractive (anisotropic), and perfectly colorless.[1] As to further reactions it may be mentioned that hot water produces a shortening and simultaneous thickening of the bundles; while no change is caused by cold water. A digestion of collagenous bundles is brought about by pepsin and trypsin in acid solution. Finally there are different methods of dissolving the cement substance lying between the collagenous fibers so that the bundles fall apart into their separate elements; lime water or baryta water act in this way, also picric acid and osmic acid. It is supposed that the cement substance between the fibers is similar to mucin. As far as their small diameter permits definite determination the fibers are cylindrical or nearly so.

In general collagenous fibers are stained by acid dyes; however there is no selective staining method for collagenous tissue which is absolutely free from objection. Neither Van Gieson's acid fuchsin—picric acid method, nor Mallory's staining with aniline blue, nor other so-called connective tissue stains, show collagenous fibers only.

The **elastic** fibers form the second variety of the fibers of connective tissue and stand in marked contrast to the collagenous fibers. Elastic fibers always form nets but never bundles; and to this end are branched in most pronounced fashion. Furthermore they are not all equally thick as is the case with collagenous fibers but their diameter varies extraordinarily; the finest are even thinner than the collagenous fibers, the thickest (ligamentum nuchae of the ox) attain a diameter of 10 or even 12 μ. But these are only a few of the differences. As regards chemical behavior, the elastic fibers are extremely resistant to reagents; they are not attacked by acetic or other acids, nor by caustic potash, nor by hot water; in all of which points they contrast with collagenous fibers. They are easily stained selectively by specific stains, especially by resorcin-fuchsin, and by orcein, so that in preparations demonstration of even the finest elastic fibers may be made without difficulty. The two kinds of fibers differ in physical properties just as widely; elastic fibers as the name implies are highly extensible and upon cessation of the extending force return to their resting position. In addition elastic fibers have color of their own; they are yellow; but in microscopic preparations the color is indistinct in the individual fibers unless they are thick, when it is somewhat noticeable. Furthermore they are highly refractive and hence are distinctly in evidence in fresh preparations, especially after the employment of

Pl.5, Fig.1
Pl.6, Figs.1,3
Pl.23, Fig.2
Pl.24
Pl.75, Fig.3

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[1] The double refraction of collagenous fibers is best investigated with the aid of the polarization microscope; but this is not the place to describe the appearances observed. Under low magnification connective tissue bundles, especially the larger, appear peculiarly dark and yellowish brown; but this appearance has nothing to do with the real color of the fibers.

acetic acid which causes the collagenous fibers to disappear optically. They are not at all doubly refractive, or are so to only a slight extent; but become so upon being stretched. Naturally they do not yield gelatin upon boiling and will not dissolve at all in boiling water except under special conditions. The substance of which they consist is named ELASTIN and is also soluble with difficulty. In forming their networks the elastic fibers bifurcate repeatedly, giving off or receiving weaker branches; and this may occur in such exaggerated form that the small-meshed net becomes a fenestrated membrane. Elastic fibers behave toward digestion somewhat differently from collagenous fibers. They are easily dissolved by pepsin in acid solution while trypsin dissolves them in the presence of alkalis. Elastic fibers vary from cylindrical to greatly flattened, bandlike forms.

Examined in the fresh condition elastic fibers appear bright, with dark contours and form a contrast to the faint, weakly refractive, bundles of collagenous fibers. The thinner the fiber is, the more closely do the dark lines which mark its edges approach one another; with the result that a hasty glance gives the impression that the elastic fiber is a single, dark streak. Very commonly the fibers, which were in netlike connection with one another, are torn through, or apart; then they curl up spirally. But this form is not normally a characteristic of elastic fibers; they are perfectly straight so long as their natural, netlike connections are not destroyed.

The meshes of the nets formed by elastic fibers are of very different widths; in ordinary, loose, unformed connective tissue they are large; with long smooth unbranched fibers forming the boundaries; in other cases of broad nets with narrow meshes the strands are short between branches. These narrow-meshed nets, especially when the
Pl.7, Fig.4 fibers which form them are broad and flat, pass into the so-called FENESTRATED MEM-
Pl.23, Fig.3 BRANES such as are constantly met with as elastic structural elements in the walls of large arteries. These membranes must be considered as narrow-meshed nets whose flat fibers have broadened, making the meshes smaller and smaller until many completely disappear. The remaining meshes are then larger or smaller holes, the "windows" of the membrane. There are thus formed thin, flat membranes of the same substance (elastin) as the fibers, having here and there small openings; only occasionally can remains of the fibers be still recognized in the homogenous elastic sheet. Naturally such fenestrated membranes have the same physical properties as the elastic fibers. When the tubular vessel, in the walls of which they occur, is in the contracted state fenestrated membranes usually appear bent like a corrugated iron plate. Occasionally, but not in man, elastic tissue appears in the form of granules, which are not the products of the destruction of fibers; although the latter may disintegrate into granules.

Close networks of very fine elastic fibers in a few cases form basal membranes (membranae propriae) which otherwise usually consist of reticulum fibers. Thus Bruch's membrane of the chorioid coat of the eye is a purely elastic membrana propria, the so-called stratum elasticum supracapillare chorioideae.

Pl.7, Fig.6 The third variety of the fibrous elements of connective tissue is usually designated
Pl.53, Figs.2,5 as **reticulum** fibers; the name of precollagenous fibers is also used, but is probably based
Pl.59, Fig.6 upon a false supposition. Since these fibers — in contrast to the collagenous and elastic fibers — may be demonstrated by silver impregnations they have also been appropriately termed ARGYROPHILE fibers.

This type of fiber is widely found in connective tissue, at least in connective tissue proper; however reticulum fibers never form clear-cut, compact masses of tissue. They are certainly more closely related to collagenous than to elastic fibers; and in many places they pass into true collagenous fibers; yet morphologically at least, they differ fundamentally from the latter. In the first place they do not form bundles but are interwoven in lattice-like fashion and frequently form true nets; and furthermore their thickness varies within considerable limits. Bifurcation of the fibers occurs beyond any doubt. There are thus a number of morphological characteristics which they share with elastic fibers but they do not consist of elastin, nor do they possess the physical properties of the elastic material, extensibility and high refractive index. They are best distinguished from the other varieties of connective tissue fibers by their argyrophile reaction; *i. e.* they are colored black by Bielschowsky's silver impregnation method, while collagenous fibers are colored yellowish-brown. Otherwise they are, in general, demonstrated by the same staining methods which color collagenous fibers; but may be distinguished from elastic tissue, for the stains which are selective for the latter do not tinge reticulum fibers. In general reticulum fibers are more resistant to reagents than are collagenous fibers; they are attacked but slightly or not at all by alkalis, do not swell in acids, and in addition like collagenous fibers are gradually dissolved by pepsin in the presence of acids, but are not dissolved by trypsin in either alkaline or neutral solution. They do not yield gelatin upon boiling.

The name of reticulum fibers is given them from their presence in reticular connective tissue (p. 72) for they represent the special type of fiber of this tissue and in it some of the fibers attain a greater diameter than usual. They form the interstitial tissue of both exocrine and endocrine glands where, so to speak, there is no room for the development of collagenous tissue with its bundles of fibers. The first to be recognized were the reticulum fibers of the hepatic lobules; *i.e.* the fine fibrils, interwoven like a lattice, which are situated around the cords of liver cells. In a more netlike arrangement they fill the extremely narrow spaces between the convoluted tubules of the kidney. In many other glands they are demonstrable as very fine extensions, so to speak, of the interstitial tissue. Where heavier masses of connective tissue occur they are formed entirely of collagenous fibers and the reticulum fibers pass immediately into the latter, so that it is often taken for granted that reticulum fibers may become transformed into collagenous fibers. Moreover the masses of cells in glands of internal secretion of the "epithelial corpuscle" type are wrapped around by the finest of argyrophile fibrils; they also occur in the thyreoid gland, and are present in many mucous membranes, *e. g.* that of the intestine.

Pl.7, Fig.6
Pl.53, Fig.5
Pl.59, Fig.6

Almost without exception basal membranes, hyaline membranes etc., are formed of reticulum fibers woven together in dense, feltlike fashion. Such connective tissue membranes usually have sharp outlines and upon them rest the superficial epithelia, including the epidermis; they also form the external layer (the so-called membrana propria) of the walls of the terminal secreting parts of glands. At the same time the tissue of these membranes is quite devoid of cells; reticulum fibers in general are usually accompanied by very few cells. At first the membranes appear homogeneous, hence the name hyaline membrane, as applied to that of the hair follicle; they stain uniformly without recognizable fibrous structure. Only silver impregnation and a few other methods, such as Traina's staining, will show up the fibers and the feltlike constitution of the membranes. Among these membranes is to be reckoned the basal membrane of the corium upon which the epidermis rests; the sarcolemma of the striated muscle fibers; the membranellae between the smooth muscle fibers; and the basal membrane of the capillaries upon which the endothelium rests. In the last example the composition of the membrane from a network of fibers is especially distinct. The same is true of the membrane of the cells of

Pl.8, Fig.8

adipose tissue which is likewise formed of reticulum fibers (p. 68). Reticulum may act as the pathway for blood vessels just as does collagenous tissue; *e. g.* within the hepatic lobules and in the brain.

The existence of a fourth class of fibers, PRE-ELASTIC fibers, is much disputed. Such fibers differ in many regards from true elastic fibers; *e. g.* they do not stain selectively with the same stains; but otherwise their behavior is much the same. Here probably belong the posterior basal membrane (Descemet's membrane) and the elastic fibers of the substantia propria of the cornea.

As already mentioned, there is in connective tissue beside the cellular and fibrous constituents a **ground substance,** which fills up the spaces that yet remain between the fibers and cells. In the embryonic mesenchyme before it contains fibers this ground substance is a fluid; and later as the fibers gradually are formed it remains between them, often to quite a considerable amount, and may acquire a more or less mucuslike quality.
Pl.6, Fig.7 Without doubt the mucuslike cement substance (p. 59), by means of which the fibers of the connective tissue bundles are held together, belongs to the ground substance; which, moreover, fills up all the clefts and spaces not occupied by cells or fibers. This ground substance is a homogeneous, amorphous material which either fills without interruption all the space of the connective tissue to which it belongs; or, as is maintained for loose unformed connective tissue, appears as separate lamellae or membranes, which may, or may not, be connected.

Naturally the question arises as to the genetic relationship in which the elements of connective tissue stand: the cells, the fibers and the ground substance. There is no doubt that in the fully formed condition all three constituents as a rule occupy positions which are quite independent of one another; thus the cells are not in connection with the fibers, and both cells and fibers merely lie in the ground substance. However there are assertions to the contrary, which declarre that throughout life fibers are connected with cells, being, so to speak, intracellular. That may, perhaps, be the case for some of the reticulum fibers which appear to be intracellular in reticular tissue. Probably the fibers (all fibers ?) of connective tissue arise either from or within cells (hence the term fibroblast p. 54) and only subsequently do most of them become independent. They are derived from an external protoplasmic layer of the cytoplasm in which during their early condition they lay enclosed. It is doubtful whether fibers can increase in number after they have left the cells which formed them and entered the ground substance, or whether fibers can arise from the ground substance (which is very unlikely). These questions have received very different answers.

We have thus become familiar with the individual structural elements of connective tissue and may now turn to the different forms in which connective tissue proper occurs in the human body. The following varieties may be distinguished: 1. Gelatinous connective tissue, 2. unformed, loose connective tissue, 3. formed connective tissue, 4. elastic tissue, 5. adipose tissue, 6. reticular connective tissue or reticulum.[1]

Gelatinous Connective Tissue

The name of gelatinous, or mucous, connective tissue is applied to a type of connective tissue which is no longer present anywhere in the adult human body, but is to
Pl.7, Fig.5 be considered as kind of older embryonic connective tissue. It is still found at the time of

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[1] Pigmented connective tissue, known also as pigmented tissue, is not specially enumerated with the above since fundamentally it is distinguished from non-pigmented connective tissue only by the pigment content of its fibrocytes; thus there is both unformed or loose, and formed pigmented connective tissue.

birth in the umbilical cord where it forms the so-called Wharton's jelly; and still later in the tissue of the enamel pulp of growing teeth. As stated it is an unfinished formation of connective tissue, in which matured elements have already appeared but have not assumed their final arrangement. The fibers met with in gelatinous connective tissue are usually already grouped in irregularly formed bundles, and are exclusively collagenous fibers, which however lie singly or in quite irregular distribution, not as yet forming compact bundles. The cells of gelatinous connective tissue are almost exclusively fibrocytes of considerable size, with few processes and of very flat form; consequently seen in profile they appear "spindle-shaped". Along with them there occur wandering cells but only in uniformly small numbers.

Unformed (Loose) Connective Tissue

a. Ordinary Loose Interstitial Connective Tissue

Pl.6, Fig.1 and many other Figures

Unformed, loose connective tissue is extremely widespread in the human body; it separates neighboring organs from one another, for instance as intermuscular connective tissue it separates the individual muscles; it forms the plastic tissue of the submucous coat of the digestive tract separating the mucous membrane from the muscular coat; it constitutes the subcutaneous tissue, although here it is largely replaced by adipose tissue. In addition it is found between the middle and the outer coats of the eyeball and in many other places. Before all else, where it occurs it guarantees the possibility of movement upon one another of the parts which it separates. Conceiveably it plays an important rôle in the nourishment of the neighboring organs; furthermore it reacts promptly to stimuli of all kinds, especially to those of pathological nature.

All of the types of cells mentioned above share in the formation of this tissue: fibrocytes, wandering cells, histiocytes, eosinophilic cells, mast cells, and in smaller numbers than the others, plasma cells; while isolated cells of adipose tissue are constantly found. Collagenous fibers occupy the first place among the fibrous elements, forming bundles of very different thickness; while numerous elastic fibers are constantly present and are often quite stout. The ground substance is present in relatively large amount.

That which is essential in the structure of this variety of connective tissue is the ability of the fibrous bundles to suffer displacement, for this "filling-in" tissue cannot have a rigid texture. Thus in the microscopic picture of this tissue the bundles of collagenous fibers now lie parallel and again cross each other at the most varied angles; now they lie close together and again they are pressed far apart according to the tension or pressure exerted on the tissue. What has been said concerning the masses of collagenous fibers is also true for the elastic tissue, the networks of which show larger meshes on distention than when the tissue is compressed. In general the meshes of the nets of elastic fibers are large in loose connective tissue, so that the real netlike structure appears only in preparations of large extent. The elastic fibers by no means follow the fibrous bundles but cross them in the most varied directions.

The ground substance of loose connective tissue appears to be lamellar (p. 62). Of the cells the fibrocytes are very flat, with rounded outlines and often very blunt processes; no regularity is to be recognized in their arrangement. They commonly lie on the fibrous bundles, frequently clasp them with their processes, and show grooved impressions on the surface in contact with the fibers, *e.g.* fine grooves produced by elastic fibers. On the other hand it is recognized that the fibrocytes are frequently situated entirely within the ground substance; so to speak within cavities in this substance, cavities whose form may be easily shown by the method of "silvering" (p. 30). This method gives a "negative" picture of the cell in which the form of the latter is more clearly seen than in the positive picture. The negative picture is usually larger than the positive because around the cell there is a pericellular space which separates it from the ground substance. Pl.6, Fig.7 Of the remaining cells of loose connective tissue all that is essential has already been mentioned in discussing the separate types of cells found in it. In some localities of the body, but particularly in the eyeball, loose, pigmented, connective tissue is to be found.

b. The Connective Tissue of the Serous Membranes

Pl.5, Fig.1 A second type, differing considerably from ordinary, loose, interstitial connective tissue is that of the serous membranes, especially of the mesenteries and great omentum. In many regards it is a transition to formed connective tissue. Its fibrillar constituents are, in the first place, connective-tissue bundles of somewhat variable size, but sharply marked off from one another; these intersect in various directions. The elastic fibers are of all degrees of fineness and form relatively narrow-meshed nets. The netlike arrangement of the elastic tissue shows nowhere more clearly than in surface preparations, for instance of the mesentery, or of a part of the great omentum, *e.g.* of the rabbit, which usually is thin and contains little fat. Generally two flat elastic nets include between them the fibrous bundles along with the homogeneous ground substance in which they lie. The cellular constituents of this type of connective tissue are numerous and varied; those of the great omentum excel in both regards. In the discussion of the cells of connective tissue it has already been pointed out that perhaps with the exception of mast cells, all the types of cells of connective tissue are present in abundance in the great omentum. Since many of these cells have phagocytic powers it cannot be wondered at that the great omentum is highly qualified to catch, as it were, foreign material; a fact which may be shown experimentally. It is true that the great omentum consists in part of a further variety of unformed connective tissue, namely of

c. Areolar Connective Tissue

The name areolar connective tissue is given to a very delicate fabric formed of net- Pl.6, Fig.4 works of connective tissue bundles, the nets having larger or smaller meshes. The fibrous bundles represent the cords of the network; in places they are thick, and again by branching they become thinner, at last they may become so fine that they no longer give lodgement to fibrocytes. The meshes between the strands of connective tissue, are filled by fluid. The finer cords of the net consist entirely of collagenous fibers; only in the thicker cords are there a few elastic fibers, as well as blood capillaries, both of which also are lacking in the finer cords. As already mentioned the finer strands of areolar connective tissue arise from the larger as branches, and from these in turn come the finest of all. After a longer or shorter course as a cord of the net they pass over into another correspondingly thicker cord in order to fuse with it. In this way they form curves around the small meshes but never encircle one completely. The boundaries of a mesh are thus always formed by several branches from larger bundles.

This areolar connective tissue is found in the great omentum where it forms the parts which are thinnest and poorest in cells. For in the region of the fibrous bundles which bound the meshes few cells are to be found except fibrocytes, a contrast to the abundance of cells in the omentum elsewhere. Both this and the previous type of connective tissue, like ordinary loose interstitial connective tissue, are very frequently replaced by adipose tissue. Naturally the surfaces of the serous membranes are covered by the peritoneal epithelium.

d. The Connective Tissue of the Inner Meninges

In the inner meninges, particularly in the so-called arachnoid membrane but also in the pia mater as well, there is found a peculiar arrangement of connective tissue bundles in part similar to that of the great omentum. That is to say the fine strands and plates which connect the two limiting lamellae of the inner meninges and cross the subarachnoid space, consist of fibrous bundles around which are woven fine nets of elastic fibers. The limiting lamellae of the inner meninges, both on the side toward the dura mater and on that toward the brain substance, recall in their structure the connective tissue of the serous membranes, and in part areolar tissue. On the surface of the strands of connective tissue, and consequently upon the nets of fine elastic tissue which surround them, there is a covering of flat endothelium-like cells. It has already been mentioned that in this connective tissue, especially at the base of the brain, scattered cells are present which contain melanin pigment.

This structure of the arachnoidal trabeculae gives occasion to an artificial appearance. If the collagenous substance swells within the elastic net from treatment with acetic acid, it sometimes happens that some of the elastic fibers are torn apart. Those which remain untorn may cause ringlike constrictions on the swollen bundles because they have not themselves swollen under the action of acetic acid. In this manner are formed the so-called laced bundles.

Formed (Dense) Connective Tissue

Formed connective tissue is distinguished from unformed, especially from loose interstitial connective tissue, by the arrangement of the bundles of collagenous fibers. In the unformed type this is highly variable; but in formed connective tissue there is a strict and constant regularity in the arrangement of the parts of the tissue, so that shifting or displacement of the fibrous bundles cannot take place. At the same time the bundles may be arranged in many different ways, but they are always bound together into firm, often very dense, membranes, cords etc. of connective tissue. In addition formed, or fibrous, connective tissue is often much poorer in cells than the unformed; the varieties of cells other than fibrocytes occur in very small numbers and only as it were by exception. Indeed the number of fibrocytes in many cases is small; this is especially so for the firmer, more compact types of connective tissue.

Formed connective tissue occurs very commonly with an interwoven arrangement Pl.5, Fig.3
of its collagenous fiber bundles, the so-called **dense, woven connective tissue;** and is Pl.6, Figs.2, 3
seen in very typical form in the corium of the skin, and in somewhat less pronounced form Pl.78, Fig.1
in the external coat of the eyeball, especially in the sclera, and also in many mucous membranes. In addition to collagenous fibers a variable number of elastic fibers participate in forming this fibrous connective tissue. Thus in the corium, fine fibrous bundles lie side by side in parallel arrangement and form, so to speak, coarser bundles which then run in all different directions. At the same time the bundles lie close together and are interwoven in the most intimate way. For the most part an arrangement of the coarser bundles parallel to the surface is recognizable, and in the lower vertebrates it is much

more regular than in man. In addition to the bundles of collagenous fibers placed thus closely together there is a small quantity of ground substance filling the narrow spaces between the coarser bundles; and also a close network of elastic fibers, many of which are quite strong. At the knots of this network indications of fenestrated membranes may appear (p. 60).

Although all types of connective tissue cells may occur in the corium, and in fibrous Pl.6, Fig.2 connective tissue in general; yet the fibrocytes outnumber the other forms which assemble chiefly in the larger clefts around the blood vessels. The sclera of the eye is of similar structure, only it is decidedly poorer in elastic fibers, which also are thinner and form wide-meshed nets; the same applies to the dura mater.

In the eye the ground substance or substantia propria of the cornea deviates somewhat in structure from the above, yet is to be considered a dense woven connective tissue. Especially does the pronounced mucinlike quality of the substantia propria of the cornea Pl.78, Fig.2 distinguish it from other connective tissue formations; *e. g.* that of the sclera into which it passes at its margin. It consists of parallel lamellae which in turn are formed of flat fibrous bundles; all the bundles of each lamella run in the same direction, but in different lamellae the directions are quite different. Between the lamellae there lie fibrocytes which are noticeably flat and are arranged at rather regular distances; they are also characterized, at least in many animals, by great regularity in their anastomosing processes (p. 54). They lie in special cavities in the mucuslike ground substance.

The fibrous connective tissue of the mucous membranes shows a decidedly less dense interweaving of its bundles; furthermore it is rich in fibrocytes and other forms of connective tissue cells. Frequently dense woven connective tissue shows a transition — usually quite gradual — into other types, *e. g.* into ordinary loose connective tissue.

Another form in which dense fibrous connective tissue appears is that of **tendinous tissue;** *i. e.* the specially dense fibrous tissue of which tendons and related structures are composed and which thus even forms organs, such as the tendons. In its simplest form this tissue appears in the tendons themselves, which are composed of bundles of collagenous fibers all running parallel; indeed a sharp and complete delimitation of the Pl.9, Fig.1 bundles in a tendon cannot usually be determined. A small tendon is, so to speak, a Pl.27, Figs.3, 4 single, thick strand of collagenous fibers between which lie fibrocytes, the only cells present in tendons; the cells thus serve, however incompletely, to mark the limits of the bundles. It is also questionable whether the presence of a true ground substance in tendinous tissue can be admitted. Of course the tendons of the human body, especially the larger and thicker tendons, consist of a large number of such thick, so-called primary, bundles. (See the chapter on the microscopic anatomy of the muscular system.) Elastic fibers are almost entirely lacking in the tendons; only a few fibers, and those delicate ones, are demonstrable.

But most of all the cells of tendons, usually known as tendon cells, require notice. Fig.10 Naturally they are fibrocytes, the only type of cell which occurs in tendons; and in man, Pl.9, Figs.1, 2 as compared with other mammals, their number is noticeably small. As already mentioned they lie in the coarser, so-called secondary tendon bundles which are, so to speak, heavy cordlike masses of parallel collagenous fibers indistinctly marked off into smaller primary bundles by the processes of the tendon cells. The cells accommodate themselves to the spaces available and as a result may have widely different forms. In cross sections of tendons they appear to be star-shaped; the rays of neighboring stars seem to anastomose and thus to mark off the primary tendon bundles from one another. In reality the rays of the stars are thin plates which extend into the spaces between the primary bundles of the collagenous fibers, but do not reach the corresponding projections from the neighboring cells. Thus for the most part the fibrocytes of tendon do not stand in direct connection with one another.

If tendon cells are regarded from the surface they appear to be flat structures which are obviously arranged in rows with only short intervals between the members of a row. Frequently within a row two neighboring cells will be seen to have their nuclei close to adjacent ends; this is probably the result of both cells having arisen through the division of the one mother-cell. The cells may be rectangular in shape, rhombic or trapeziform, or even irregular. The nucleus, which is also flat, shows no essential peculiarities; while the cytoplasm is pronouncedly basophile in staining. Seen edgewise the tendon cell appears almost like a line, due to its extreme thinness. In surface view one, or more rarely two, fine lines appear upon the cell. This is due to one or two processes of the cell projecting more or less at right angles to the surface. If such a Ranvier's tendon cell taken from a tendon in the tail of a mouse, or of a rat, is very regular in form, four winglike, flat processes will project from its surface; hence the appropriate name of tendon wing-cell. Two of the processes lie in the plane in which the cell is flattened, and the other two project perpendicularly to this plane. It is the latter which appear as lines upon the surface of the cell, and in cells of regular form the line is exactly in the middle. Of course perfect regularity in the form of the cell is rare; especially in man quite irregular forms of the cell occur, with only three, or with more than four processes. Naturally the processes are seldom at even intervals, often the "line" does not lie over the middle of the cell but more toward one edge.

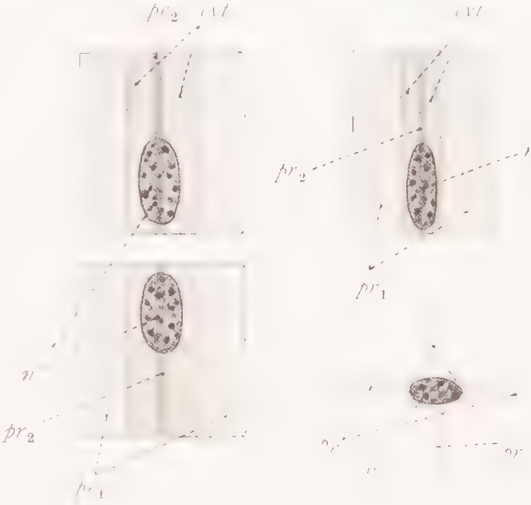

Fig. 10. **Diagram of a Tendon Wing-cell.**

Left; two cells seen from the surface; upper right a cell seen from the edge; lower right a cell seen in cross-section.

cyt = cytoplasm of the main part of the cell
pr = processes of the cell
pr^1 = surface view of a process
pr^2 = edgewise view of a process
n = nucleus or nuclei

The fibrous membranes such as aponeuroses, fasciae, the tunicae albugineae and connective-tissue capsules of many organs, the dura mater, periosteum and perichondrium all belong to tendinous tissue; but occasionally approximate in character dense, woven connective tissue. In exceptional cases the arrangement of the collagenous fibers, which play the leading rôle in the composition of these structures, is as regular as in the fascia lata of the frog, where a rectangular crossing of two layers of collagenous fibers occurs; usually the arrangement is decidedly irregular. Just as in tendons, fibrocytes alone are present and elastic fibers are infrequent, yet now and then the latter occur in rather large quantity; thus the periosteum, and the tunica albuginea of the corpora cavernosa penis have quite abundant elastic fibers.

It can be understood that many structural arrangements of connective tissue do not fit exactly into anyone of the foregoing groups; there are many kinds of transitions from one to another.

1, a. Elastic Tissue

While the types of connective tissue previously described may be called connective tissue in the narrower sense; the varieties of tissue now to be described differ so greatly in many regards that they bear a special name, one from which the term "connective" is omitted. Among them belongs elastic tissue. It is distinguished from connective tissue Pl.9, Fig.3 proper by having the elastic connective tissue elements in it, which are mostly fibers, predominate over those of collagenous or reticular nature. Indeed the quantity of elastic fibers may be so great that the collagenous and other tissues appear only as a supporting tissue. This is the case, for example, in the ligamentum nuchae of the ox (there is no true ligamentum nuchae in man), which is formed of heavy elastic fibers up to 12 μ in diameter, arranged parallel to the long axis of the ligament and to one another. But the separate elastic fibers, close as they lie and near to one another as they come, never quite touch but are always separated by collagenous or reticulum fibers. As in all other situations (p. 59) the elastic fibers form networks in the ligamentum nuchae. In isolating the fibers it is seen that they have branches which come off at acute angles and connect with neighboring fibers; only in this case the meshes are elongated to an unusual degree and are of minimal breadth, really only clefts. The small amount of tissue which separates the individual elastic fibers of the ligamentum nuchae is, for the most part, not collagenous tissue but consists of reticulum fibers. The finest strands of this tissue are perfectly free from nuclei; but they gradually pass into somewhat stronger collections of connective tissue in which lie the scanty blood vessels of the ligament. In this tissue there lie also nuclei of fibrocytes and here the tissue takes on the character of true collagenous material (p. 67). The elastic fibers of the ligamentum nuchae are not all of equal thickness; while the larger as said, measure 12 μ, many others are less, down to a thickness of 3—4 μ. In any case the ligament consists only of elastic fibers of very considerable thickness; in some places they are cylindrical, in others distinctly flattened, still others appear in cross-section to be even triangular with rounded corners.

Fundamentally therefore, elastic tissue, even in its purest form such as occurs in the ligamentum nuchae, differs only in degree from ordinary connective tissue. In addition to occuring in the ligamentum nuchae a similar arrangement of tissue is found in the ligamenta subflava of the vertebrae, the ligamentum vocale of the larynx and some other ligaments in the body; but in no case does the proportion of elastic fibers equal their proportion in the ligamentum nuchae, nor is their strength as great.

In a somewhat less pure, and so to speak, less evident form, elastic tissue occurs in the Pl.23, Fig.3 walls of the large arteries; but in place of elastic fibers there are present elastic lamellae or fenestrated membranes. However as a matter of fact, even in these cases the elastic tissue predominates over the collagenous.

1, b. Adipose Tissue

A peculiar type of connective tissue — in the wider sense — which presents a quite different picture from ordinary connective tissue is that known as adipose tissue. It is Pl.7, Fig.1–3 very widely distributed in the human body although the extent of its development varies considerably in different individuals. In this connection it becomes apparent that almost everywhere in the human body ordinary, loose interstitial connective tissue may pass into adipose tissue. Fat cells, either isolated or in larger or smaller groups, occur in the interstitial tissue of many glands, such as the lachrymal gland and the salivary glands.

Since adipose tissue is a storage tissue, in which the excess of nourishment is stored in the form of fat, the amount of it varies with the supply of food. If the latter is considerably increased, adipose tissue is observed to appear where otherwise only connective tissue free from fat is to be found; and if conditions are reversed, as in starvation, adipose tissue disappears from situations in which its presence is normal.

However there is a series of localities in the body in which adipose tissue occurs in compact masses, except under conditions of great and pathological emaciation. Outstanding examples are the subcutaneous tissue, especially that of the palm of the hand, the sole of the foot, and the buttocks, and the fat surrounding the kidney and in the mesentery etc. Special local accumulations of adipose tissue form the retrobulbar adipose tissue of the orbit of the eye, Bichat's fat-pads of the cheeks, the appendices epiploicae of the large intestine etc. In addition the so-called yellow marrow is adipose tissue.

The character of adipose tissue is determined by the FAT CELL; for it is the only variety of connective tissue in which the cells so greatly predominate over the fibrous constituents of the mass that on first impression the latter seem largely to have degenerated or almost to have disappeared. The fat cell is, so to speak, the fibrocyte of adipose tissue, but it takes the form of a storage cell and as such reaches a considerable size, usually 60—80 μ but exceptionally 40 or 120 μ. Its form is that of a sphere,[1] or at least it is approximately spherical; however it is clear that neighboring cells are somewhat flattened by mutual pressure. When adipose tissue is examined in the fresh condition it appears as a mass of strongly refractive spheroidal structures lying close together; they seem to be quite amorphous and further examination in the fresh condition gives no information as to their structure. As a consequence of death the amorphous material may be replaced by crystals of fatty acids.

In fixed preparations after staining etc. the following constituents appear to be distinguishable in the fat cell: first the so-called fat-cell membrane, a fine membrane which covers the surface of the entire sphere. It is most clearly in evidence when the fat has been dissolved out of the cell, as happens to the great majority of permanent microscopic preparations through the use of strong alcohol, xylol etc.; so that as a rule fat cells are seen in this state. Secondly the nucleus of the cell is seen surrounded by a very little cytoplasm which appears applied to the inner surface of membrane. The entire remainder of the fat cell, as seen in the section, is empty; here lay the fat droplet, once stored up but now dissolved out in the course of preparation. The large size of the fat cell is solely and only determined by the droplet of fat stored up in the cell. Pl.7, Fig.2

Formerly the structure of the fat cell was explained as follows: the fat cell is derived from the ordinary connective tissue cell, the fibrocyte (a conception which is correct, at least in part). Fat is laid up in the cytoplasm of the cell, appearing first as separate droplets which then fuse producing one large drop. The latter distends the cytoplasm so strongly that except for a small amount around the nucleus there remains only a thin film-like covering, the so-called fat cell membrane. According to this view the fat cell membrane would be the superficial part of the greatly distended cytoplasm; it cannot be a true cell membrane for animal cells do not have true cell membranes p. 14).

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[1] The description of the fat cell which follows is that which was formerly customary. For understanding the microscopic structure it is chiefly to be recommended on didactic grounds; actually the structure of the fat cell is rather different.

Naturally the nucleus is greatly flattened against the membrane of the cell and becomes concave. Quite uniformly the nucleus of the fat cell contains from one to several small fat droplets. When the fat is dissolved the openings, really vacuoles, left in the flattened nucleus produce the so-called perforated nucleus of fat cells.

The fat droplet may be retained undissolved in preparations in which it has been blackened by osmic acid solution, a measure which makes it insoluble if the after treatment is careful. Or dyes which stain fat may be used and reagents which dissolve it avoided; such preparations must be preserved in glycerine. Upon examination both of fresh material and of that which has been acted upon by osmic acid the fat droplet in all cases appears homogeneous. It is neutral fat, a glycerine ester of the higher fatty acids (stearic, palmitic, and oleic acids) in variable combinations. The consistency of the fat depends upon which acid predominates, oleic acid giving a soft fat, and stearic acid a hard one. Only in cells Pl.7, Fig.3 of adipose tissue taken in decomposition after death, does a splitting into glycerine and Pl.7, Fig.1 free fatty acid occur, a splitting which takes place very easily in neutral fats. In such cases there appear within the fat drop needle-like crystals often arranged in star shaped form, the so-called margarin, or oleo-margarin crystals.

Actually the conception of the structure of the fat cell set forth above no longer corresponds to the facts obtained through the newer methods of investigation. Before going into these a glance must be taken at the fibrous constituent of adipose tissue; for although the cells predominate in adipose tissue, of course there are also fibrous elements present. Considering first the larger ordinary accumulations of fat, it is clear that septa of collagenous connective tissue mark off large groups of cells which lie close together. In the septa there are found ordinary fibrocytes, and to some extent other types of connective tissue cells as well, along with small pre- or post-capillary vessels. Between the fat cells themselves only capillaries are to be found. Such a mass of fat cells lying closely pressed together and separated from other similarly arranged masses of fat cells by ordinary loose interstitial connective tissue is termed a LOBULE OF ADIPOSE TISSUE. This lobular structure may be recognized in almost all the larger accumulations of fat. True collagenous tissue does not enter into the lobule, but fibers of reticular tissue fill the extremely small intervals between the individual fat cells. After the fat has been dissolved out in making a permanent preparation, that which gives the impression of being the fat cell membrane is really a membrane formed of reticulum fibers woven together. The question often arises whether the fat droplet lies bare against this membrane thus leaving the trifling amount of cytoplasm around the nucleus to represent the former cytosome; Pl.7, Fig.2 or whether to the inner surface of the membrane of reticular tissue there is applied a delicate border of protoplasm. If so the thickness of the border must be too slight to be measurable.

At a certain stage of embryonic life there is as yet no fat cell in the whole body of the embryo; but the question as to the formation of a fat cell from a connective tissue cell which does not contain fat, receives at present rather different answers. It must first be recalled that fat cells arise at a definite stage of embryonic life; that later, and indeed as long as life lasts, they may be formed from connective-tissue cells; thus the red marrow gives origin later on to the adipose tissue of the yellow marrow. It must also be borne in mind, that where in youth adipose tissue is lacking or scanty, in later years there often occur considerable accumulations of fat, as for instance beneath the serous membranes;

also that embryonic accumulations of fat later on may degenerate in part; *e. g.* Bichat's fat-pads. Thus adipose tissue is never formed primarily as such, but always from another variety of connective tissue, which may still have an embryonic character as when adipose tissue is formed in the embryo; but fat cells may also arise from fully developed connective tissue. Without doubt different types of connective tissue may serve as the basis for the post-embryonic formation of adipose tissue; for while it usually is seen to arise from ordinary interstitial connective tissue, it is derived from reticular tissue in the transformation of red into yellow marrow.

Since without doubt the cells of reticular tissue differ from the fibroblasts of fully developed connective tissue in being of more embryonic character, it may be assumed that the formation of adipose tissue from reticular tissue would be almost equivalent to its embryonic formation. However there is no doubt that fat cells may be formed from ordinary connective-tissue cells which are already specifically differentiated; in the midst of connective tissue isolated fat cells are to be seen. On the other hand it is very probable that the first trace of adipose tissue in the embryo is derived from complexes of connective-tissue cells which have not at all reached final differentiation into true fibrocytes. The cells which become transformed into adipose tissue are those of relatively indifferent embryonic connective tissue. There is reason for the recognition of embryonic adipose-tissue organs which so to speak have the task of forming adipose tissue in the embryo. This manner of the formation of fat cells would agree with their formation from reticular tissue in the marrow of bones. In this process it must not be assumed that the disposition to form net-like cell connections is retained; it is very probable, a priori, that in storing fat a cell assumes a spherical form and draws in its processes; indeed the fat cell membrane formed from reticular tissue suggests that the cell itself has no processes.

Just as fat may be stored up by connective tissue cells originally free from it, so it may be given out again by the fat cells when formed; the fat being a reserve material to be used in the economy of the body under conditions of inadequate nourishment. Fat is believed to enter the embryonic cells in split and saponified form; while after birth it reaches the cells unsplit as the haemoconia of the blood. In many animals the warehouses for fat in the fat cells are thus filled and used up periodically. A typical example is the tail of the fat-tailed sheep in which enormous amounts of fat are stored while nourishment is abundant, to be completely consumed later in the year when food is lacking. This removal of the fat converts the typical fat cell into a serous fat cell. In storing fat the cell first forms small fat droplets, then larger ones which finally fuse, while at the same time the quantity of cytoplasm visibly diminishes. In the transformation of the fat cell into the atrophic form, the serous fat cell, the mass of the drop of fat does not simply diminish but breaks up again into isolated droplets like vacuoles. In serous fat cells such as are found constantly in the atrophic bone marrow of old age, the so-called gelatinous marrow, the nucleus is again found in a central position and the remnant of the fat as isolated droplets in the cytoplasm. Apparently the last remnants of fat are later removed from the cell which had already grown smaller and at last contains only serous or mucous material in its vacuoles. Phagocytic leucocytes may share in the removal of fat from the serous fat cells.

Cells which have thus lost their fat may store it up again, as happens periodically in the case of animals. But that does not mean that a serous fat cell becomes again an indifferent connective-tissue cell or perhaps a true fibrocyte. The masses of adipose tissue which periodically fluctuate in size are certainly to be considered as organs of adipose tissue in the sense described above. After starvation they consist of accumulations of small serous fat cells which because of their lessened size are no longer so striking as are the typical fat cells. Because the fibers again predominate the tissue now gives much the impression of ordinary connective tissue, except as it differs through the abundance of cells and particularly from the presence of the serous fat cells in mass.

1. c. Reticular (Connective) Tissue

Pl.5, Fig.7 Pl.7, Fig.6 The last type of connective tissue, in the wider sense, to be discussed here is the so-called reticular tissue, or reticulum. This is a form of connective tissue which never occurs alone but only as the supporting tissue of the so-called adenoid organs. It forms the foundation of adenoid or lymphatic tissue; which is not a properly tissue at all but consists of lymphocytes, one of the varieties of colorless blood cells (p. 88), suspended as it were, in the meshes of reticular tissue. Adenoid tissue enters into the composition of lymph glands, spleen and related organs. Reticular tissue is best seen in its typical form as a netlike fabric if frozen sections of the adenoid organs are cut, and shaken out in water. Since the lymphocytes have no real connection with the reticular tissue they can be dislodged from its meshes by shaking, if the sections are sufficiently thin.

Reticular tissue is a primitive and little differentiated form of connective tissue which probably comes directly from the embryonic mesenchyme. The tissue is relatively rich in cells which form distinct nets of rather small meshes and which must be regarded as fibrocytes. It was long mistakenly assumed that the reticular nature of the tissue depended only upon the anastomotic connections of its cells. They form a net the meshes of which are rather small, averaging in diameter from 20 to 40 μ but varying somewhat beyond these dimensions. To these cells there is added the fibrous part of the tissue in the form of reticulum fibers (p. 60), which indeed bear this name just because of their presence in this tissue. These fibers show all the characteristics previously described; they bifurcate, the coarser fibers dividing into finer ones; the branches interlace in lattice-like fashion and also form true nets. Apparently these fibers support the cellular network and give it the necessary firmness; they form the framework requisite for the reception of the lymphocytes which are lodged in the tissue.

These reticulum fibers stand in most intimate relation to the cellular network; they adhere to the cells and follow most closely the course of their anastomosing processes. The resulting impression is that they actually lie within the marginal zone of the cytoplasm of the cells.

On the other hand it is possible that the fibers lie in grooves on the cells and their processes, and are not truly intracellular. Apart from everything else it is quite conceivable that here in reticular tissue the fibers really occur in an intracellular position, since according to the origin of connective-tissue fibers (p. 62) this is their primary position. From the primitive character which reticular tissue retains throughout life it is highly probable that the fibers do not become independent. However the fibers of reticular tissue may show a high degree of independence, indeed they often give rise to formations which are perfectly free from cells.

2. Cartilage

Pl.8, Figs.1–4 Pl.9, Fig.4 The second chief type of supporting, or connective, tissue is cartilage. In the adult human body it does not play so important a rôle as it does in many lower vertebrates, in which it not only occurs more extensively than in man but also shows more numerous varieties. In embryonic life, and to some extent in youth, cartilage is more widespread than in the fully developed organism in which it is almost entirely replaced by bone.

In general, cartilage is distinguished from the other varieties of supporting tissue by its peculiar consistency. Its hardness resembles that of bone, though much inferior; but at the same time it may be cut and is flexible unless, of course, it has been calcified. However there are non-cartilaginous formations of similar physical porperties such as the so-called cartilage (tarsus) of the eyelid, many interarticular cartilages of the joints and so-called fibro-cartilaginous formations such as that of the pubic symphysis etc. All these are purely connective tissue structures and transition forms from true cartilage to dense connective tissue. Consequently in deciding as to the presence or absence of cartilage the critical point is not the consistency of the tissue but its histological structure. This is characterized by two features; in the first place the cartilage cells, the only cells (fibrocytes) in the material, have no processes and as a result cannot form cell nets. They may occur singly or in groups. The closed spaces in which these cells are lodged are known as the cartilage lacunae. In the second place cartilage is distinguished by the ground substance or matrix in which the cells are situated.

In the human body only three varieties of cartilage are to be distinguished; this is in contrast to the lower vertebrates, and also to many mammals in which still other types of cartilage are to be found. The three varieties referred to above are closely related and pass into one another without sharp boundaries; they are 1. hyaline cartilage, 2. elastic cartilage, 3. fibro-cartilage. The first variety occurs more extensively in the human body than the others, and particularly so during youth and embryonic life. It is also to be considered as the most primitive form.

Hyaline Cartilage

Hyaline cartilage derives its name from the translucent quality of its ground substance or matrix, which in thin layers is almost transparent. It appears to be homogeneous and colorless, or it may show a faint bluish white tinge. It exhibits many characteristic properties. In the fresh condition it usually appears upon examination to be entirely structureless and quite transparent. It is more or less distinctly stained by basic dyes, such as haematoxylin which gives it the characteristic blue appearance so familiar in microscopical preparations. Fibrous structures are rarely to be recognized, and then only at a definite age of the cartilage. In spite of this the matrix of hyaline cartilage contains great quantities of collagenous fibers and upon boiling yields considerable quantities of gelatine; but it is a cartilage-gelatine or chondrin, somewhat different from the gelatine of fibrous tissue. The reason why the fibrillar structure of the matrix is not to be recognized in the microscopic picture is that the matrix contains an acid, chondroitin-sulphuric acid, which causes the collagenous fibers to swell, just as does acetic acid (p. 59). The refractive index of the fibers is thus lowered to that of the cement which unites the collagenous fibers. They are said to be "masked". The same acid also causes the matrix of hyaline cartilage to stain with basic dyes, while elsewhere collagenous substance shows an affinity for acid stains. Consequently where the amount of collagenous fibers is large and that of the matrix is small, as at the margin of a piece of cartilage, the matrix becomes oxyphilic like other collagenous tissue. Pl.8, Figs.1, 2 Pl.9, Fig.4

That cartilage matrix consists of collagenous fibers and of a cement which holds them together is most clearly shown by digestion experiments upon cartilage, using trypsin etc. The matrix which formerly appeared so homogeneous then falls apart into dense masses of fibers because the cement has been digested away. Treatment with potassium permanganate or with baryta water also brings out the fibrous structure of cartilage.

In hyaline cartilage of very simple structure the matrix shows not the least indication that it consists of collagenous fibers or even contains any of them; it appears absolutely clear and transparent. Such cartilage may easily be observed in the surviving condition in sections cut from the head of the femur of a frog. In other cases, as in the cartilages of the human ribs in which the matrix is considerably less transparent, parallel, straight fibrous elements are seen, the so-called asbestos-like structure of cartilage.

Taking a glance at the CARTILAGE CELLS before discussing the peculiarities of the matrix, it appears that but a single type of cell is present in cartilage; these cells must Pl. 8, Fig. 1 be considered as the fibrocytes of the tissue. They lie in the matrix in cavities known as CARTILAGE LACUNAE. These spaces are completely filled by the cells so that the size of the cartilage lacuna and that of the cartilage cell is exactly the same. This again is seen very clearly in sections of surviving cartilage from the head of the femur of a frog. The form of the cartilage cell varies, usually it is polyhedral with rounded edges, not infrequently it is somewhat flattened, and occasionally very greatly so. Flattening is very clearly seen when two or more cartilage cells lie in a common lacuna; in such a case the surfaces of contact are usually flattened against each other. The cartilage cell is an unusually sensitive structure, the form of which easily changes under the action of even the most delicate reagents. Except in the above mentioned preparation from the frog, or a similar preparation suitable for examination in the surviving condition,[1] there is rarely an opportunity of observing cartilage cells which are intact and not shrunken. The peculiarly delicate structure of the cell depends upon the exceptional quantity of water contained in the cytoplasm. If the water is withdrawn the cell shrinks and its surface becomes more or less indented; and what is still more noticeable, it retracts from the wall of the lacuna and gives rise to a quite artificial pericellular space.

Fine droplets of fat are regularly found in the cytoplasm of the cartilage cell, glycogen is abundant; and both plastosomes and a circumnuclear reticular apparatus may be demonstrated. The nucleus is usually spherical or approximately so, and may be seen with especial distinctness in the surviving cell if physiological salt solution is used in the examination; it shows no peculiarities worth mentioning. The cartilage cell has no processes whatever, structures which might be considered as such are artefacts. In exceptional cases there do occur branched forms of cells, but in man only in a few embryonic cartilages. The term cartilage capsule, (a term which probably could well be dispensed with), refers to certain superficial formations of the cytoplasm which perhaps correspond to the formation of a crusta; according to another view the cartilage capsule belongs to the matrix.

Special peculiarities of the **cartilage matrix** are to be met only in older pieces of cartilage; young cartilage is free from such. There may always be observed, even in the highly homogeneous matrix from the femur of the frog, a narrow, and usually rather clear, area around the cartilage cells, which so to speak, forms the wall of the lacuna Pl. 8, Fig. 1 itself. But differences in the matrix are seen much more clearly when the larger hyaline cartilages of the adult body, such as those of the ribs, larynx etc. are examined. In such cases two different things are to be noted; in the first place the border zones of the matrix and of the cartilage as a whole are constituted differently from the central regions; and in the second place the latter do not show a uniform character, but certain areas differ from others, for instance as regards staining. Consequently cartilage structure has a

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[1] The gill cartilages of salamander larvae are very suitable objects for this purpose; they do not need to be sectioned but are sufficiently transparent to be examined whole.

TERRITORIAL aspect. It must also be taken into consideration that with the single exception of articular cartilages which border joint cavities with their bare substance, all the hyaline cartilages of the human body — and the same applies to the bodies of animals — are covered by a connective-tissue membrane which rests directly upon the cartilage; this membrane is termed the perichondrium.

The marginal parts of a cartilage; *i. e.* those zones of its substance which adjoin the perichondrium, are relatively poor in matrix; nor does the matrix of these zones show as elsewhere a basophilic character, indeed it is oxyphilic (eosinophilic) like the collagenous Pl.9, Fig.4 tissue of the perichondrium. Moreover toward the margin of the cartilage its cells are small and greatly flattened; they lie parallel to its surface, are more or less in rows, and in this zone only one cartilage cell lies within each lacuna. The deeper an area lies within the cartilage, *i. e.* the farther it is removed from the perichondrium, the less oxyphilic does its matrix appear and the larger do its cells and lacunae become; in particular they are less flattened than in the marginal zone. The oxyphilic margin must be regarded as young, immature cartilage; it passes over, so to speak, without sharp boundary into the connective tissue of the perichondrium. Thus cartilage increases from without by apposition (but see below).

On the other hand the inner parts of the cartilage are the older; in them the cartilage has already attained its final structure; and shows the typical phenomena of age. These internal areas of the cartilage are not alike in all the hyaline cartilages of the body but within certain limits show important variations, especially as regards the behavior of the matrix toward stains. The essential point of all these appearances is somewhat the same and is appropriately characterized in the expression TERRITORIAL ORGANIZATION. In these central parts of the hyaline cartilage which are more and more strongly basophilic the Pl. 8, Fig.2 individual cells at first increase in size. While the cells of the superficial layers of cartilage measure only about 5 μ and frequently even less, toward the center the size increases up to 30 μ. In addition the cells arrange themselves into groups of 2—6 and even many more; Pl.9, Fig.4 all the cells of a group lie in a common lacuna. These spaces lodging several cells have always an ellipsoidal form, the long diameter of the ellipse standing at right angles to the perichondral surface of the cartilage, which invariably is more or less even. In general these lacunae, and also the number of cells which they shelter, become larger toward the center of the piece of cartilage. These cell nests which are uniformly present in the central parts of hyaline cartilage are appropriately termed CHONDRONES.

Although it is predominantly basophilic the matrix in the central regions of a hyaline cartilage varies in its reaction to stains. It is not everywhere equally basophilic and in places is even oxyphilic. Immediately around the lacuna is a zone, the cartilage capsule (but see above), which is usually narrow and very strongly basophilic. Next follows as a rule an inner area which is also basophilic, but less strongly so. Such weakly basophilic areas usually include several lacunae and their cells. Around these basophilic, inner areas there may now appear correspondingly larger outer oxyphilic areas; between which lies basophilic, interterritorial substance like a lattice or network. However there are cartilages in which the interterritorial matrix is strongly oxyphilic while both the inner and the outer areas previously mentioned show a basophilic character; the inner less than the outer which holds basic dyes very strongly.

In the central parts of such large cartilages as those of the ribs there are found areas which contain remarkably few cells and cell nests (chondrones). Here also occurs that type Pl.8, Fig.2 of formation already mentioned in which parallel fibers produce an asbestos-like striation in the matrix. The scarcity of cells in such an area is referable to the death and disappearance of many of those originally present. Increase in the bulk of a hyaline cartilage occurs not only at its surface from the perichondrium (growth by apposition), but also throughout its interior as growth by intussusception. Embryonic cartilage, the so-called pre-cartilage, consists of a concentration of mesenchyme cells, it is rich in cells and poor in matrix; but gradually the amount of the latter increases as the cells secrete matrix, and become pressed further apart in consequence. In young, actively growing cartilage, the cells divide mitotically; the daughter cells at first are close neighbors but are soon separated from one another by the matrix which they secrete. In older cartilage the daughter cells lie nearer one another and form the cell nests; still later amitotic division is said to be frequent. Along with this late formation of new matrix within hyaline cartilage there may also occur the subsequent death of the cells.

The phenomenon of double refraction in hyaline cartilage is due to the collagenous fibers in the matrix. These fibers do not form true bundles as in connective tissue; for the most part they lie strictly parallel throughout extensive areas although the direction of the fibers differs on the surface of the cartilage from their direction in its interior. In the superficial zones marked by small cells and little matrix, the direction of the fibers is parallel to the surface. On the other hand in the central parts the direction is determined by the groups of cells; here the fibers run perpendicular to the surface. In many cartilages there may be recognized systems of fibers arranged according to quite definite architectonic principles.

Cartilage is entirely devoid of blood and lymph vessels. This is in sharp contrast to connective tissue proper which not only contains blood and lymph vessels but carries them for the tissues which have none; *e. g.* epithelium (p. 33). Cartilage also is devoid of nerves; nor are wandering cells ever found in cartilage although they penetrate deeply into epithelial tissue. The nourishment used by cartilage is indeed carried by blood vessels but it proceeds exclusively from the perichondrium. To nourish a thick piece of cartilage, it may be imagined, is a difficult matter, for lymphatic canaliculi do not really exist although they have occasionally been described. The central regions of cartilage are reached by what must be a slow, tedious process of diffusion through the cement substance between the fibers. Consequently these regions can suffer marked disturbances of nutrition showing as asbestiform degeneration of the matrix and the death hof cells.

It has already been mentioned that hyaline cartilage is more widespread in the body during youth than in adult life. This is true in still greater degree of the embryonic body since nearly all the elements of the embryonic skeleton which later become bone consist at first of hyaline cartilage (p. 135). Of these skeletal cartilages of the embryo there remain permanently only the articular cartilages, the cartilages of the ribs, the large laryngeal cartilages, the greater part of the cartilage of the nose, the tracheal cartilages and those of the two bronchi; while the arytenoid cartilages and those in the wall of the bronchial branches show a transition to elastic cartilage.

Hyaline cartilage may become calcified by the deposition of salts of calcium in the matrix, exactly the same process as occurs in bone, see p. 80. Usually, especially in the embryonic cartilaginous skeleton, such calcification marks the commencement of a later ossification which replaces the calcified cartilage by bone; at the same time blood vessels enter into the skeletal part. Calcification also precedes the formation of bone in the partial ossification which always occurs in the larger laryngeal cartilages.

Elastic Cartilage

Pl.8, Fig 3

Elastic cartilage is distinguished even macroscopically from hyaline cartilage by its pronouncedly yellow color; for the elastic fibers retain in the matrix the characteristics which they always show elsewhere, viz., a yellow color and a netlike arrangement. By virtue of its elastic elements it is much more pliable than hyaline cartilage and when bent returns to its original form. In structure it is distinguished from hyaline cartilage principally by the occurrence in the matrix of elastic fibers as well as those of collagenous nature. With increase in the amount of elastic tissue the peculiarities of elastic cartilage (color, etc.) become more distinct. Otherwise the constitution of elastic cartilage is exactly like that of hyaline cartilage, apart from the peculiar territorial features already mentioned; but even these may differ in individual hyaline cartilages. Amongst other things the cells of elastic cartilage are wholly like those of hyaline cartilage, they lie in lacunae in the matrix etc., but usually form smaller groups.

Thus the essential feature distinguishing elastic cartilage is the presence of elastic fibers, which may be either fine or coarse. In man the fibers are usually fine, or even very fine, and as a rule form networks of very close and narrow meshes, especially in the central areas of the cartilage. The elastic fibers are always least numerous in the marginal parts of the cartilage where they pass directly into the rather abundant elastic fibers of the perichondrium. Elastic fibers are easily demonstrated by specific stains, whether they occur in elastic cartilage or in other tissues. Even in cartilages rich in networks of elastic fibers there is always some hyaline matrix containing collagenous fibers. Where there is a transition from the one type of cartilage to the other and nearly related type, nets of elastic fibers appear, which at first are few and of large mesh but which become progressively denser, more numerous and of closer mesh. The amount of hyaline matrix diminishes proportionately. An elastic cartilage is apparently always formed from a primary hyaline cartilage so that its younger zones are always the poorer in elastic fibers. According to the content of elastic fibers or of collagenous fibers sections of elastic cartilage show a more or less distinctly blue stain with haematoxylin (p. 73). Unlike the hyaline variety elastic cartilage never becomes calcified.

The occurrence of elastic cartilage in the human body is decidedly more restricted than is that of hyaline cartilage. It forms the auricular cartilage of the ear and the smaller laryngeal cartilages, the cartilage of the Eustachian tube and of the external acoustic meatus. Elastic cartilage which passes without sharp demarcation into hyaline cartilage is found in the processus vocalis of the arytenoid cartilage, and in the cartilaginous plates of the bronchial branches of medium and smaller size. However in the latter situations both elastic and hyaline varieties are always found combined.

Fibro-cartilage

Pl.8, Fig.4

That which used to be called fibro-cartilage, or white fibro-cartilage is properly not at third variety[1] of cartilage at all, but is a mixture of tissues consisting of densely fibrous, formed connective tissue containing scarcely any cells, with islands of cartilage scattered throughout it. These islands consist of cartilage cells singly or in quite small groups surrounded only by cartilage capsules.

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[1] Indeed since hyaline and elastic cartilage differ only in degree and pass by transitions into one another, there is properly speaking only a single type of cartilage in man.

Fibro-cartilage is not very widely distributed in the human body and where present it often passes into purely fibrous tissue. Its occurrence is restricted to numerous articular discs, labra glenoidalia, the annuli fibrosi of the intervertebral discs, and to many symphysial cartilages. It passes on the one hand into purely fibrous tissue free from cartilage, and on the other into true hyaline cartilage, as in the intervertebral fibro-cartilages. Since the fibrous part is usually entirely devoid of cells the formation of fibro-cartilage is probably to be thought of as derived from true hyaline cartilage by increase in the quantity of fibers and diminution in the number of cells.

As already briefly mentioned there are still other forms of cartilage, especially among the lower animals. Among mammals beside the forms described there is the so-called cellular cartilage containing very little matrix which is found in the ears of rats and mice. In man also it is found in very small quantities along with purely fibrous tissue in the insertions and sesamoid bones of certain tendons and is known as vesicular supporting tissue or chondroid tissue. It is composed of vesicular cells between which is a minimal quantity of matrix, apparently like that of hyaline cartilage.

There are also to be found in man during youth some scanty remains of the embryonic notochord. Because of its embryonic origin the notochord cannot be regarded as a connective-tissue structure (p. 52); yet by virtue of the vesicular character which its cells assume, especially in the lower vertebrates, it has the consistency of cartilage. Remnants of it persist in the nucleus pulposus of the intervertebral discs and are still recognizable in the newborn as a group of vesicular cells which later degenerate. In the adult only very indistinct remains of the former notochordal cells are to be found.

3. Bone

Bone tissue, which composes almost all the skeletal elements of the human body, and the closely related dentine of the teeth are the hardest of all the human tissues. The enamel of the teeth is still harder, but it is not truly a tissue. The great hardness of bone is due to salts of calcium deposited in its matrix. For bone like cartilage is composed of matrix and cells; the latter, again as in cartilage, lie in lacunae in the matrix. Nevertheless cartilage and bone are two entirely different varieties of supporting tissue which can never become converted the one into the other. Bone does indeed replace cartilage, but in doing so the cartilage, after previous calcification (p. 76) must be dissolved and removed before bone can be formed in its place. No cartilage, not even calcified cartilage, can be directly transformed into bone, and obviously it is still less possible for the reverse process to occur.

The salts of calcium which give hardness to bone are found exclusively in the matrix where they occur in variable amounts so that there are harder and less hard varieties of bone (or of bones since they consist chiefly of this tissue). The salts of calcium may form up to 70% by weight of bone but the proportion is usually less, often considerably so, down to 55%. Of this percentage the larger part is calcium phosphate, some is calcium carbonate while calcium fluoride is present in very small amount. The bone may be freed of these salts of calcium by the process of decalcification, *i. e.* by treatment with acids, of which hydrochloric and nitric acids in diluted form are the most used. The bone which previously was too hard to be cut has now about the consistency of cartilage and may be sectioned. For this decalcified bone the term ossein has been employed. Under such treatment bone loses 50—70% of its weight. On the other hand by carefully heating bone to redness its organic constituents are removed; in this case the decrease in weight is correspondingly less. Under neither process dœs there occur a diminution in volume. As a result of this peculiarity in its structure bone may be examined either in sections cut after decalcification or in slices which have been ground thin after maceration. The pictures obtained by these two different methods of preparation must be combined in order to obtain an understanding of the structure of bone.

As regards its CELLS, bone like cartilage contains but one type of cell, which is to be considered as a fibrocyte; and also like cartilage it encloses its cells in cavities in the matrix. But it differs from cartilage in that its cells, briefly known as OSTEOCYTES, are branched and connect with one another by anastomosing processes; a distinction from cartilage which naturally extends also to the bone lacunae. Bone cells are exceptionally delicate and are utterly destroyed by maceration, consequently they can only be examined in decalcified bone and best in that from young individuals. They appear as extremely delicate structures, entirely devoid of a membrane, and are usually elongated. Their form is more or less markedly flattened in one plane. Generally there can be clearly seen projecting from each cell a number of processes by which it connects with its neighbors. The cells contain spherical nuclei, often somewhat flattened but without further peculiarities. The foregoing is essentially the condition in adult or lamellar bone; in the reticulated bone of the embryo and of the early years of life the lacunae and cells are irregularly spherical with little or no flattening.

Pl.9, Figs.5,6

Pl.21, Fig.5

Pl.22, Fig.5

The cavities in the matrix in which these cells lie are termed BONE LACUNAE. They are studied much better in the empty condition, *i. e.* in ground preparations of macerated bone, than when filled by their cells. In the ground preparations they contain air and under the microscope appear white by reflected light and black by transmitted light because in the latter case a total reflection of the light occurs from the narrow air-filled spaces. Unless the bone cell becomes shrunken from the injurious action of reagents it, like the cartilage cell, exactly fills its lacuna, consequently the form of the bone cell is most readily studied from that of the lacuna to which it belongs. In adult bone the lacunae are usually long, flat and curved, their position and arrangement in the matrix will be dealt with later. The length of the lacunae varies from about 18—40 μ, the breadth from 8—15 μ, the thickness from 4—8 μ. From the lacunae there run fine tubules scarcely 1 μ in diameter, but in some cases of considerable length depending upon the distance between the bone cells. Although they branch their course is rather straight. By means of these BONE CANALICULI the neighboring lacunae stand in connection with one another.

Pl.19, Figs.1, 2

Pl.20, Fig.2

The bone cells are so extremely sensitive and have so little ability to resist injury from the process of decalcification that it is difficult to observe them intact in permanent preparations. Consequently certain proof that the bone cells completely fill the lacunae, and particularly that in general their processes fill the canaliculi is not to be obtained. Nevertheless there is hardly the least doubt that such is the fact in young bone. It is possible that in older bone where the cell processes have become very delicate some of them may disappear and that the connection of neighboring cells through their processes is broken here and there. But there is no change in principle concerning the relations of the bone cells; the assertion that in adult bone the cells die and leave the lacunae empty is not proven.

Pl.9, Fig.6

The MATRIX of bone stands in contrast to the bone cells; it alone is calcified. It contains the fibrous elements of bone, those which yield the gelatine; for upon boiling bone yields ossein, a variety of gelatine. Bone matrix, like cartilage matrix, consists of collagenous fibers and ground substance in the narrower sense. The zones which form the immediate boundaries of the lacunae and canaliculi are distinct from this matrix and are known as

Pl.20, Fig.4

BONE CAPSULES. They are free from fibers and the substance of which they consist resists acids, so that if a ground section is treated with acid they remain while the rest of the matrix is dissolved. They may thus be isolated from the true matrix. Apparently they do not become calcified(?).

According to the relations of the collagenous fibers two kinds of matrix may be distinguished: 1. lamellar matrix which almost without exception is the type found in the adult organism; 2. reticular or coarse-fibered matrix which is almost entirely confined to embryonic life. **Lamellar matrix** (the term lamellar bone is also used) is characterized in the first place by having its collagenous fibers formed into very fine bundles consisting Pl.20, Figs.3,4 of from six to eight fibers only. The individual bundles are separated from one another by thin zones of ground substance free from fibers. Such matrix is formed into lamellae or leaves which have a thickness varying from 5—12 μ but usually are from 7—10 μ. They Pl.10, Figs.1,3 are chiefly arranged in small concentric rings around the canals which contain the blood vessels of the bone; these are known as Haversian lamellae (p.132). There also occur superficial lamellae which lie parallel and close together. In each lamella there lies a single row of lacunae containing bone cells. In lamellae which are sharply curved, like those Pl.20, Fig.1 around the canals of narrow caliber, the lacunae are markedly curved on the flat and their long axis is parallel to that of the bone as a whole.[1] In any two adjoining lamellae the bundles of collagenous fibers usually run in different directions; often in concentric lamellae the directions alternate with regularity. If in one lamella the fibers run parallel to the long axis of the bone, in the neighboring lamellae they will usually — but not always — run in a plane perpendicular to this axis. All the bundles within the same lamella are always parallel.

Reticular bone with its coarse fibers stands in contrast to lamellar bone. It is essentially an embryonic form of bone tissue which persists during the first years but is rarely found in adult life. In this type of bone tissue both the collagenous fibers and the cells differ from those of lamellar bone. In the first place the cells and lacunae are noticeably larger in reticular bone and are of irregular form; moreover their distribution shows no regularity. But the outstanding feature is that the greater part of the collagenous fibers are arranged in coarse bundles although some fine bundles are to be found; and even the coarse bundles are clearly composed of separate finer bundles. These connective-tissue bundles form networks around wide and irregular spaces which contain vessels; any arrangement into lamellae is completely lacking. This type of bone is, so to speak, calcified connective tissue.

As a result of its content of collagenous fibers bone matrix is doubly refractive, as is shown clearly on examination by polarized light. Elastic fibers occur but only in small number and in the lamellae which lie close to the periosteum; otherwise they are lacking in bone. The salts of calcium occur in such finely divided condition in bone that no optical means can render them visible; it is assumed that they lie in the ground substance while the fibers are considered not to be calcified.

As already mentioned the first variety of bone tissue to appear in the embryo may be thought of almost as calcified connective tissue. For in this primitive, reticulated bone tissue the connective-tissue bundles surrounded by calcified matrix show essentially the same arrangement as in ordinary connective tissue. Special cells of the embryonic connective tissue secrete the matrix around the connective-tissue bundles which are already present or else are formed under the influence of the cells. Still later these cells also have an important role to play in the formation of bone and consequently bear the name of OSTEOBLASTS. Thus arise thin plates of young bone matrix containing collagenous fibers but at first they are completely free from cells (p. 136). The osteoblast is a cell of rounded form which contains but one nucleus and is relatively rich in protoplasm. These same cells, to which fell the role of secreting bone matrix, now become surrounded by young matrix and are known as bone cells or osteocytes. During this process they gradually relinquish the rounded form, become branched or rather develop processes which previously were not to be seen, and finally establish connections with neighboring cells. The bone cells or osteocytes are just as truly descendents of the embryonic mesenchyme as are the cartilage cells; but unlike the latter they do not proceed directly from the indifferent mesenchyme cells but pass through the intermediate stage of being osteoblasts. Pl. 21, Fig. 5 Pl. 22, Fig. 3

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[1] In transverse sections of a long bone the lacunae and bone cells are cut across; if in a longitudinal Pl.19, Figs.1, 2 section the lamellae are cut perpendicular to their surface the narrow, profile view of the cells and lacunae is seen. But if the lamellae are cut longitudinally and parallel to their surfaces then the breadth of the cells and lacunae, their greatest dimension, is exposed.

The **osteoblasts,** the true formative cells of bone tissue, are specially differentiated cells of embryonic connective tissue, which differ from the ordinary cells of the latter tissue in a number of characteristics. The rounded form and the relative abundance of cytoplasm have already been mentioned. Osteoblasts frequently show processes, although the latter are very fine and but few in number. It is characteristic of the cytoplasm of these cells to be distinctly basophilic although not to a very high degree. Usually the nucleus lies somewhat eccentrically; centrosomes, reticular apparatus etc. may be demonstrated. These cells occur in all places where bone is being formed for they supply the matrix of the bone and they themselves become the osteocytes. A surface upon which the apposition of new bone is taking place is covered with osteoblasts set close together so that they are flattened against one another like cells of an epithelium. The secretion of new bone matrix then proceeds as a rule only from one surface of the layer of osteoblasts, namely from that which is next to the young skeletal element. Osteoblasts which become embedded in the matrix as a rule become the fixed osteocytes. In later stages of the matrix these cells may die and disappear as do cartilage cells under similar circumstances. Thus in young bone a certain amount of growth may take place by intussusception, while later only growth by apposition is to be observed. Pl. 21, Fig. 5 Pl. 22, Fig. 3

In contrast to these bone-forming cells there stand others, termed **osteoclasts,** which cause the dissolution of bone. They differ decidedly in appearance from osteoblasts for they are multinucleate giant cells or polykaryocytes (p. 14) of variable but considerable size (20—50 μ). The number of nuclei varies from four to twelve and even more, the size of the cell being in proportion to the number of the nuclei. The nuclei almost always lie in a group pressed closely together. It is the part of the osteoclasts to dissolve bone matrix which has previously been calcified; they also dissolve calcified cartilage. They play consequently an exceedingly important rôle in all the phenomena of the resorption of these two tissues and in the gradual development and remoulding which the skeleton, especially the embryonic skeleton, undergoes (p. 136). An area where these cells are present in an embryonic or immature bone will be devoid of osteoblasts. If the osteoclasts are observed at a time when they are active in resorption they will be found lodged in more or less deep pits in the bone substance, pits which they have, so to speak, eaten out for themselves (so-called Howship's lacunae). At the same time the form of these cells, which during Pl. 21, Figs. 6-8 Pl. 22, Fig. 5 Pl. 21, Fig. 7 Pl. 22, Fig. 5

inactivity are commonly spherical, often becomes extremely bizarre. Where the cells lie close together they form adjoining lacunae which continually become deeper and are separated by projecting bars of bone matrix not yet absorbed. These bars are then grasped and soon undergo resorption by the osteoclasts which may be seen, so to speak, to ride their edges. Bony surfaces where such resorption has taken place consequently appear quite irregular, as though they had been gnawed. Very remarkable figures arise through osteoclasts breaking down the provisionally calcified cartilage of a developing bone (p. 136).

As regards the origin of the polykaryocytic osteoclasts, they are formed by the fusion of a number of mononuclear cells from the yet indifferent embryonic mesenchyme. Whether, after ceasing their activity in resorption, they fall apart again into single cells, or what their fate may be is yet to be determined. They probably possess powers of amoeboid movement and are drawn to the site of their activity by a stimulus which is lost after resorption has ended.

Appendix I: The Cellular Elements of the Blood

In addition to the great group of the supporting and connective tissues two other structural elements of the human body must here be discussed. Both are of purely cellular nature, their cells, like those of the connective tissues, being the direct descendents of the embryonic mesenchyme. These additional elements are, 1. the different types of blood cells and the related cells of the red bone marrow, 2. endothelium.

The BLOOD is a fluid in which float cellular elements. Consequently it is not a tissue, for its elements have no regular and recognized arrangement; its characterization as a "fluid" tissue is not justified. The fluid portion is known as the blood plasma; it is colorless and lies entirely outside the field of morphological investigation. The formed elements, mostly cells, are distributed throughout the plasma; they have long been known as blood corpuscles, a name given them before cells were discovered. Only the corpuscular constituents of the blood will here be discussed. They fall into the following subdivisions which are by no means of equal value: 1. the so-called red blood corpuscles or erythrocytes; 2. the colorless blood corpuscles or leucocytes;[1] 3. the blood platelets, also well named thrombocytes; 4. the so-called blood dust or haemoconia. The elements in 1 and 2 are cellular; those in 4 are definitely non-cellular; in 3 their cellular nature is doubtful.

The Red Blood Corpuscles (Erythrocytes)

Pl. 10, Figs. 1, 2
Pl. 11, Figs. 1, 2

The red blood corpuscles of all mammals, including man, are non-nucleated cells. They have long been known by the former name although in exact histological language the term is erythrocyte. In number they are by far the predominating elements of the blood and to them alone is its red color due, for the plasma is entirely colorless. On an average there are in man five million erythrocytes in one cubic millimeter of blood in the male, and four and a half million in the female. In the new-born, and at high altitudes, their number is considerably greater. Like all the corpuscular elements of the blood they float in the plasma and are borne along by the blood stream. They occur only in vertebrate animals,[2] which consequently have red blood, but their number, size and form differ greatly in different orders of vertebrates, even in different genera. In man, as in all mammals, although it has no nucleus, the red blood corpuscle is a true cell to the extent that it was derived from a nucleated antecedent cell by loss of the nucleus. They are very labile cells with a very short duration of life and have only a single specific physiological function, namely to take up oxygen in respiration.

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[1] Since these corpuscles are not white but colorless and transparent the former name, white blood corpuscles, should be avoided.

[2] The chordate Amphioxus has no erythrocytes.

In man the erythrocytes are structures of disclike form. Under the microscope they appear faintly greenish yellow but not in the least red; while the surface of each is quite smooth, the margin even and the edges distinctly rounded. Both surfaces are quite alike and are hollowed, *i. e.* they bear a central broad but very shallow depression. The shape of the erythrocyte affects its appearance under the microscope as follows. In surface view the red blood corpuscle appears circular with a central, ill-defined, rather dim area which is the depression. On focusing lower the picture is reversed, the border fades and becomes somewhat darker while the center grows brighter. When a thin layer of human blood is viewed under the microscope a few of the red blood corpuscles will be seen in profile and present a biscuit-like form. Human erythrocytes are plain biconcave discs. In size they are usually quite uniform, at least seventy-five to eighty per cent have a diameter of 7.5 μ. Along with these "normocytes" there also occur quite a number of erythrocytes which are either larger or smaller. The former are termed megalocytes and measure 8.8 μ; the smaller forms, termed microcytes, are only 6 μ in diameter. Larger or smaller forms than these are rare and may be pathological or artefacts. The greatest thickness of the border varies between 2.3 and 2.8 μ, the thinnest area in the depression measures only about 1.5 μ.

It is a question whether the size of erythrocytes can vary, whether under changed conditions their size alters in one and the same individual, whether external influences such as hunger etc. affect the size of the red blood corpuscles; probably such is not the case. Another question is whether or not certain departures from the form of a biconcave disc are normal. Mention will be made later of several alterations in the form of red blood corpuscles which are typical artefacts. Perhaps the same is true of the so-called BELL or hat-shaped form of erythrocyte which in certain quarters has been regarded as normal. It seldom occurs in fresh preparations of blood, but chiefly in such as have been fixed, for instance when osmic acid is employed; the red blood corpuscles then have the form of concavo-convex bowls.

There are no cells of the human body, (apart from the male sexual cells, the sperms), which are so easy to examine in the fresh, living or surviving, condition as are the cells of the blood. For their examination is made not merely in a perfectly indifferent medium but in the very same as that in which the cells were when within the body, the blood plasma itself.[1] In such a preparation the erythrocytes appear with the dimensions, form and color as given above; beyond this the red blood corpuscle appears under the microscope to be absolutely structureless and homogeneous. Yet because it is at rest this picture naturally differs from that of the corpuscle in the flowing blood within the living body. As a result pictures are seen which scarcely would appear during life but which nevertheless reveal characteristics of the erythrocytes which are significant of their physical constitution. Here in the first place belongs the phenomenon of rouleaux formation. The red blood corpuscles possess as it were sticky surfaces and thus when not swept along by the blood stream they stick together, or at least show a great tendency to do so. If the layer of blood under examination is sufficiently thick the red blood corpuscles lie partly overlapping one another in rows which are usually curved; the individual corpuscles appear to stick together. This process is appropriately termed an agglutination. In it the concave, disclike form of the

Pl. 10, Figs 1, 2

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[1] Naturally care must be taken that the blood plasma does not evaporate; otherwise it becomes hypertonic and produces great alterations in the form of the erythrocytes.

red blood corpuscle is retained. The red blood corpuscles are also flexible and elastic so that after distortion they return to their previous form.[1]

Concerning the finer structure of the red blood cell not much is known. Since it springs directly from a nucleated cell (p. 92) it must also be considered as a cell and its structure referred to the general structural conditions of cytoplasm. In the first place the red blood corpuscle has NO cell membrane as is frequently asserted. (If it did have it would be the sole exception of the kind among animal cells.) However the external layer of its cytoplasm may well be different in constitution from the interior, in particular it is free from the red[2] coloring matter which gives its color to the erythrocytes, and through them to the entire blood. This coloring matter is an iron-holding, albuminous substance, termed HAEMOGLOBIN, which is present in solution in the red blood corpuscle and is supposed to be held in the vacuole-like meshes of the cytoplasm. The latter, so to speak, forms the cords of the network and has quite improperly been termed the stroma of the erythrocyte. This delicate framework of cytoplasm becomes more and more condensed toward the surface where it forms a continuous exoplasmic outer layer, a kind of crusta.[3] By virtue of its high content of lipoids this crusta-like layer unites with many dyes and produces the appearance of a membrane.

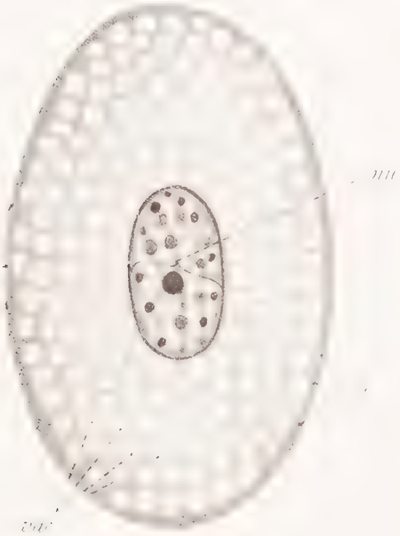

Fig. 11. **Diagram of the Structure of an Erythrocyte of the Frog.**

cr = crusta-like external layer
nu = nucleus
vac = vacuoles (to be thought of as filled with haemoglobin)

The structure of the erythrocyte as just described explains various artificial appearances which occur in preparations of blood, either spontaneously or by the intentional addition of reagents. One of the most common of these appearances is noticed in making a preparation of fresh blood if the operation is not carried through with sufficient care Pl. 10, Fig. 2 and rapidity. Under such circumstances, there is produced a spiny or CRENATED FORM of red blood corpuscle. It is the result of the withdrawal of water from the erythrocyte and consists of a more or less severe shrinkage of the crusta-like outer layer. Such figures are produced in quantity when blood plasma loses water by evaporation and becomes hypertonic to the contents of the erythrocytes. Before showing a crenated form the erythrocyte becomes spherical. Of similar nature are the so-called mulberry forms in which knoblike outgrowths appear upon the erythrocytes which remain disc-shaped.

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[1] This appearance is less frequently observed in the case of man and mammals than in the larger blood corpuscles of the amphibia which become distinctly folded during their passage through narrow capillaries etc. Observation of the circulation may be made in living animals, *i. e.* in the tail of a tadpole, in the lung of a frog or the web of its foot.

[2] As already mentioned single erythrocytes are yellowish green; not until a layer of blood attains a certain thickness does the red color appear.

[3] However this is not a membrane for it passes gradually into the remaining cytoplasm. That red blood corpuscles do not consist of a membrane and fluid contents is best shown by the fact that an erythrocyte, *e. g.* from the frog, can be cut into fragments without escape of fluid. Moreover the separate fragments show the same characteristics as does the intact corpuscle.

Of all the phenomena observed in connection with the red blood corpuscles the most frequent is that of haemolysis, *i. e.* the escape of the haemoblobin from the erythrocyte, a result produced by the action of many reagents. Since only the erythrocytes contain haemoblobin normal blood is of the nature of a "body color"; but it is easily converted into a "lake", even merely by the addition of distilled water. That is to say the water dissolves the haemoglobin out of the red blood corpuscles so that it passes diffusely into the plasma and colors it red. The blood corpuscles thus become decolorized and no longer appear yellowish green but quite pale and colorless, their contours are faint and difficult to recognize. In this condition the washed out corpuscles often receive the name of shadow-corpuscles. At the same time as they lose their haemoglobin the corpuscles alter their form and become spherical, their diameter being correspondingly diminished. Weak acids and alkalis and, in certain concentrations, the solutions of many salts act as does water; while strong alkalis preserve well the form of the blood corpuscles; and strong acids cause haemolysis with decomposition of the haemoblobin. Haemolysis is also induced by other reagents, by freezing and subsequent thawing, by electrical discharges etc.[1]

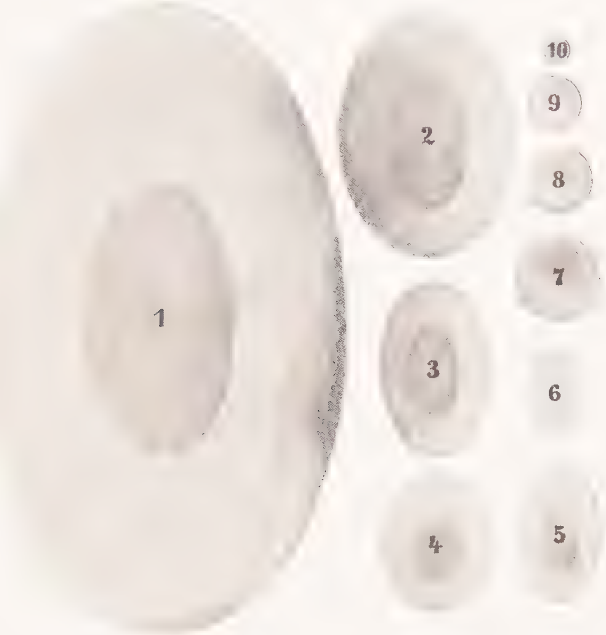

Fig. 12. **Photographs of Welcker's Models of Blood Corpuscles.** The models represent the corpuscles enlarged 1500:1. The figures after the names give the actual size of the corpuscles.

1. Proteus 58×35 μ.
2. Frog 22.3×15.7 μ.
3. Lizard 15.79×9.9 μ.
4. Tench 12.8×10.2 μ.
5. Chaffinch 12.4×7.5 μ.
6. Llama 8×4 μ.
7. Man 7.2—7.8 μ.
8. Dormouse 6.2 μ.
9. Goat 5.4 μ.
10. Musk deer 2.5 μ.

The erythrocytes of almost all mammals are like those of man. The erythrocytes of the Tylopoda (Llama, Camel) are exceptions in which the discs are elliptical, but nuclei are lacking. In most mammals the erythrocytes are smaller than they are in man, but Fig.12 in the elephant they are larger, 9.4 μ. The smallest red blood corpuscles among mammals occur in the musk deer, 2.5 μ; occasionally large mammals have quite small erythrocytes, for instance those of the horse measure only 5.5 μ. All mammalian erythrocytes lack nuclei; on the contrary those of all other vertebrates always contain centrally placed nuclei.

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[1] It is not the task of histology to deal with the action of all reagents upon the erythrocytes.

In addition the lower vertebrates (birds, reptiles, amphibia, fishes) with very few exceptions[1] have elliptical, disclike red blood corpuscles, not circular discs like those of most mammals. The elliptical blood discs of the non-mammals are not biconcave like those of mammals but are biconvex. For the nucleus, which is relatively less flattened than the cytoplasm of the cell, produces a bulging on both sides of the corpuscle. The erythrocytes of non-mammals are thus throughout their lives nucleated cells, while those of mammals are nucleated only in their early stages. The nuclei of these elliptical blood cells are of short-elliptical, moderately flattened form and show a distinct, though very delicate, nuclear network. They are free from haemoglobin and as a result are quite recognizable in the living cell. As mentioned, the nucleus produces a thickening of the central zone of the corpuscle which in profile appears as a rod thickened in the middle.

Pl. 10, Fig. 3 The nuclei of the elliptical erythrocytes become especially distinct when a slight haemolysis has occurred as during the first effects of dilute acetic acid. Naturally it also appears in the shadow-corpuscles after complete extraction of the haemoglobin, when what the observer first sees is the relatively intact nucleus; only by reducing greatly the illumination does the elliptical contour of the corpuscle become visible. By the action of vigorous reagents, perhaps aided mechanically, the nucleus can be dislodged from the cell after haemolysis.

The elliptical, nucleated erythrocytes of non-mammals vary in regard both to size and to the proportion between their long and their short axes. The largest are found in the amphibia. The fact that this order of vertebrates usually has cellular elements of maximum size is not the whole explanation for the size of the corpuscles differs greatly in different amphibia. Thus the long axis of the erythrocyte of the frog measures only 22 μ (about three times the diameter of the human erythrocyte), while in *Proteus anguineus* the measurement is 58 μ and in the American urodele, *Amphiuma means*, as much as 78 μ. The erythrocytes of birds are generally much smaller, but the ellipse is particularly long in proportion to its width. The same is true for many reptiles, in which however the blood corpuscles are decidedly larger. In the fishes the erythrocytes are remarkably short ellipses.

Naturally the smaller the erythrocytes are, the greater is their number. While in man there are five million present in one cubic millimeter of blood, in the majority of mammals, almost all of which have corpuscles smaller than those of man, this number rises to ten, twenty or even more millions. On the other hand the number is very much lower when the size of the blood corpuscles becomes excessive, *e. g.* in *Proteus* it is only 36,000.

When the blood corpuscles are very large their peculiar flexibility already mentioned becomes distinctly apparent. Large blood corpuscles, like those of the frog, can pass through narrow capillaries, particularly when the latter curve or anastomose, only by becoming bent or folded.

The Colorless Blood Cells

In contrast to the colored blood cells, *i. e.* the red blood corpuscles, the colorless cells Pl. 10, Figs. 1–4 are free from the blood pigment, the haemoglobin; nor do they show the great variety of form which occurs among the erythrocytes of the different classes of vertebrates. The colorless blood cells, the leucocytes as they have unfortunately been named, have the same peculiarities of form etc., even approximately the same size[2] in all vertebrates. Moreover Pl. 11, Figs. 1, 3–15 the colorless blood cells are by no means restricted to the blood in their occurrence, being also found in the lymph and as wandering cells in almost all tissues; the same cell is at one moment within the blood and soon afterward within the tissues. Colorless cells identical with those in the blood are also found in many organs such as lymph glands, spleen, bone marrow etc.

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[1] The red blood corpuscles of the lampreys are such short elliptical discs that they are almost circular; however they contain nuclei.

[2] This does not mean that the leucocytes of the same species of animal are all of the same size, quite the reverse. But while enormous variations occur in the size of the erythrocytes in different species of vertebrates the variation in the size of the leucocytes is relatively small.

All the colorless blood cells of all vertebrates are nucleated cells, and are not such short-lived elements as are the erythrocytes. When at rest they have a spherical form, but they are able to alter their shape when, as is generally the case, they are engaged in amoeboid movement. Like the red blood corpuscles they are descendents of the cells of the embryonic mesenchyme but do not appear in the embryo until much later than the erythrocytes. While all erythrocytes are the same type of blood cell, the colorless blood cells — leucocytes in the widest sense — fall into two markedly different groups

As regards their relations in HUMAN BLOOD the colorless blood cells are decidedly fewer in number than are the erythrocytes; moreover in contrast to the latter their number varies greatly even in the same individual at different hours of the day. During hunger fewer leucocytes are usually found than during digestion. In one cubic millimeter of human blood there are as a rule from five to seven thousand colorless blood cells; however the number may fall considerably below five thousand or rise to ten thousand even though no pathological condition is present. In pathological conditions the number may rise very considerably. There are thus from eight hundred to one thousand erythrocytes for every leucocyte present in the blood. In man the size of the leucocytes varies between the extremes of 5 μ and 20 μ, the great majority lying between 10—12 μ; consequently as a rule the colorless blood cells are larger than the red blood corpuscles, although there do occur some of smaller diameter. This does not hold for animals with quite large erythrocytes, *e. g.* the amphibia; for while the leucocytes, like all the cells in such cases, are larger than in man and in mammals yet all the varieties of leucocytes, large as well as small, are in general smaller than the erythrocytes. As already mentioned, the leucocyte when at rest is spherical in form.

The colorless blood cells are among the most primitive cells in the bodies of men and animals. The faculty of amoeboid movement belongs only to them and to nearly related cells; while that of phagocytosis, is associated with them in the great majority of cases, although not exclusively so. This and the progress of both phenomena as seen in these cells under the microscope have already been set forth (p. 18).

If the colorless blood cells are examined under the microscope in a thin layer of blood, such as will lie between slide and coverglass, they are found as a rule to be sparsely scattered among the numerous erythrocytes visible in the preparation. Pl. 10, Fig. 2 They are distinguished from the erythrocytes at once by their lack of color; they are truly COLORLESS (not at all white), and usually are more or less transparent. In many colorless blood cells in the fresh condition the nucleus cannot be preceived at all, but as a rule it is seen very indistinctly in the middle of the cell as a clearer area which stands out distinctly if acetic acid be added. The cytoplasm shows various appearances; it may be almost perfectly homogeneous and transparent; again, particularly under dark field examination, it displays certain structures like the finest of granules or rods, or perhaps droplets like vacuoles; in certain cases strongly refractive granules may be seen, often in large numbers.

The colorless blood cells swell under the action of water; their cytoplasm becomes so altered as to give the impression that the cell is surrounded by a membrane and has extremely fine granules for contents. These granules for the most part show under the microscope dancing movements, the so-called Brownian molecular movement, a purely physical not a biological phenomenon.

Within a colorless blood cell there can be demonstrated numerous plastosomes and Pl. 10, Fig. 4 a centrosome from which a radiation extends widely into the cell; however the radiation is usually observed clearly only in amphibia. The characteristics of the nucleus and of the cytoplasmic inclusions, which vary so greatly in the different forms of colorless blood cells, are particularly worthy of note, since they supply the basis for the subdivision of the colorless blood cells, leucocytes in the wider sense, into two chief groups.

Thus the colorless blood cells of one of the two chief groups will differ markedly from those of the other group as regards nucleus, size, and granular inclusions in the cytoplasm; in addition there is a very small third group. The two main groups are termed, 1. leucocytes in the narrower sense or polymorphonuclear leucocytes,[1] and, 2. lymphocytes. The differences are as follows: as regards numerical proportion the leucocytes in the narrow sense are by far the more common, comprising about 74% of all colorless blood cells, while the lymphocytes make up only 22—24%. The polymorphonuclear leucocytes are moreover of greater size, than the erythrocytes, usually 10—12 μ but rising in some cases to 14—18 μ. The lymphocytes are decidedly smaller with diameters varying between 5 μ and 8 μ; thus at their largest they equal the size of the red blood cells but mostly are considerably less. Finally the nuclear features are very different. The small lymphocytes have spherical nuclei which are large, often strikingly large, and very rich in chromatin. Nor does the size of the nucleus depend upon the varying sizes of the cells; on the contrary the smallest forms have just as large nuclei as do the largest of the group. The nuclei of the polymorphonuclear leucocytes on the other hand are relatively small in bulk and are also polymorphous (lobulated etc.). Thus while in the lymphocytes the bulk of the nucleus is strikingly large in proportion to that of the cytoplasm, in the leucocytes the bulk of the cytoplasm is always much the greater. To this very decided difference there is added another; the scanty cytoplasm of the lymphocyte shows no granular inclusions while the cytoplasm of the polymorphonuclear leucocyte is distinguished by exceedingly characteristic granules.

Pl. 11, Figs. 1, 3–5

The small **lymphocytes** with round nuclei represent the smallest variety of colorless blood cells. In the circulating blood they are decidedly less common than the cells of the other main group; but to make up for this they have a very wide distribution outside of the blood and should very probably be regarded as the most primitive type of colorless blood cell. For instance they are much more common in the circulating blood of the lower vertebrates and even in the blood of children they make up almost 50% of all colorless blood cells. Their most essential characteristic is the possession of a strikingly large nucleus the size of which may be so great that in the smaller cells it is surrounded by only a narrow border of cytoplasm. The nucleus of the lymphocyte, as may be imagined, is much easier to recognize in the living cell than is the polymorphous nucleus of the living leucocyte. In addition it stains much more intensely with basic dyes which means that it is richer in basichromatin than is the nucleus of leucocytes. The abundance of chromatin accumulates as coarse droplets on the inner surface of the nuclear membrane producing the so-called "wheel" nucleus (p. 10). The cytoplasm is definitely basophilic although not strongly so. It is possible by special methods to demonstrate granular structures — so-called azurophilic granules — in the cytoplasm of lymphocytes but they are not comparable to the specific granulations of the polymorphonuclear leucocytes. Corresponding to the small amount of cytoplasm in the smaller forms of lymphocytes their power of amoeboid movement is slight although doubtless it is present, for lymphocytes occur as wandering cells in various tissues as well as in the blood. Their most important occurrance is in forming, so to speak, the parenchyma of adenoid organs — lymph glands, spleen, tonsils and related structure, and probably also the thymus — where they lie embedded in reticular connective tissue. In these organs also are to be found the centers for the increase in number of the lymphocytes.

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[1] Another term, "granulocyte", has recently met with much favor. It is open to objection as an etymological hybrid but so are other and well recognized terms, *e. g.* "polynuclear" and "neutrophile". — Translator's note.

The POLYMORPHONUCLEAR **leucocytes** stand in contrast to the lymphocytes. A relatively small nucleus which is more or less deeply lobulated is common to them all. Indeed the lobulation may be so extreme that at first glance the leucocyte appears to have a number of distinct and separate nuclei; but threads of chromatin, be they ever so fine, are always present as connections between them. Beside points of difference previously mentioned the cytoplasm of leucocytes always contains peculiar granular inclusions, the behavior of which, especially toward dyes, varies. Using these reactions to dyes as a basis the polymorphonuclear leucocytes (or granulocytes) are divided into three groups: first those with neutrophilic granulation, second those with eosinophilic (or better oxyphilic) granulation, third those with basophilic granulation. Those of the first group are by far the most common; of all colorless blood cells 70% in round numbers contain neutrophilic granules; those with eosinophilic granules are decidedly more rare making up 2—5%. The basophile leucocytes are very scarce, about ½%, and are only to be found in the circulating blood, whence the appropriate name blood mast cells (p. 57).

Pl.10, Figs.2, 4
Pl.10, Figs.1, 7–10, 15

The leucocytes with NEUTROPHILIC granules, the commonest of all the colorless blood cells, are 10—12 μ in diameter. Only a small percentage fails to show deeply lobulated and highly polymorphic nuclei. The cytosome is almost or quite filled with very fine granules of approximately uniform size which, as the name implies, show a neutral reaction although they can also react to either acids or alkalis. Their refractive index is very low and they are rendered visible only in specially stained preparations made by definite mixtures of dyes. They show great powers of amoeboid movement during which they send out extremely fine pseudopodia (p. 18). Their power of phagocytosis is equally great. Outside the blood they occur normally as wandering cells and pathologically as pus corpuscles.

Pl.11, Fig.1

Polymorphonuclear leucocytes with EOSINOPHILIC granulation are relatively rare in the circulating blood but in the living condition, even without staining, their highly refractive granules easily distinguish them from the leucocytes with neutrophilic granulation. In addition the eosinophilic granules are coarser than the neutrophilic but not so closely set. They are very resistant to reagents, *e. g.* acids, and stain readily with all acid aniline dyes. The eosinophile leucocytes are usually larger than the neutrophile (12—14 μ). Whether the granules contain iron and are connected with the destruction of red blood corpuscles is very uncertain. These cells show amoeboid movement and occur as wandering cells (p.54).

Pl.10, Fig.2
Pl.11, Figs.12–14

The leucocytes with BASOPHILIC granulation, the mast cells of the blood, are most extremely rare in the circulating blood (½%). Their granules, like those of the eosinophile leucocytes just mentioned are coarse and highly refractive; but at times their size is not uniform nor their distribution regular; often they are not closely set in the cytoplasm. In size the cells are usually not large (10—11 μ); the nucleus is commonly polymorphous, but in contrast to that of tissue mast cells it is never highly so. The granules show exactly the same behavior as do those of the tissue mast cells with which however they are not supposed to be identical; hence the name blood mast cells (p. 57).

Pl.11, Figs.15, 16

The third chief group of colorless blood cells is that of the large **mononuclear** leucocytes, still better termed monocytes. They represent the largest type of the colorless blood cells and measure 14—20 μ in diameter. They are uninuclear cells with abundant cytoplasm in which the nucleus generally lies in a slightly eccentric position. Usually the nucleus is elliptical, often with a depression on one side, but it is never polymorphous. For

Pl.11, Fig.11

the most part it shows extremely little affinity for basic dyes and does not stain deeply. The significance of the cells and their relation to the other colorless blood cells is not yet fully determined; however they show amoeboid movement and are conspicuously phagocytic. In contrast to the small wandering cells which show phagocytic activity and have been termed microphages these monocytes are known as MACROPHAGES.

It is doubtful whether there are transitional forms between the various groups of colorless blood cells although certain pictures could be so explained. The point is bound up with the question of the derivation of the colorless blood cells; whether these so to speak, have a common origin or come from two perfectly distinct sources. In the latter case the pictures mentioned are to be accepted as of areas engaged in the formation of the non-granular lymphocytes on the one hand and of the granulocytes on the other. There is not the least doubt that the chief seats of the formation of lymphocytes are the lymphatic or adenoid organs. In the germinal centers (p. 149) of the lymph glands, the splenic corpuscles, the various tonsils, and perhaps also in the thymus, new lymphocytes are continually being formed which entirely correspond to those of the circulating blood. From the lymph glands they pass into the lymph and so into the blood, while those which are formed in the spleen pass directly into the blood stream. Only those produced in the tonsillar structures reach neither the lymph nor the blood but traverse the epithelium (p. 204). Granulocytes are not formed in the places mentioned; the seat of their formation is rather the red bone marrow which will be treated later. Nevertheless the question is open whether the non-granular lymphocytes with round nuclei which, as was mentioned, are beyond doubt the most primitive forms of colorless blood cells and which are much more numerous during youth, may not later become transformed into polymorphonuclear forms with granules; particularly since all transitional forms between spherical and polymorphous nuclei are found. That granules can form within non-granular colorless blood cells is beyond doubt, for all granular leucocytes are derived from non-granular mother cells; to which it may be added that the nature etc. of a granule does not by any means always appear to be the same even though its staining reaction gives the same result.

Blood Platelets

Although the blood platelets, or thrombocytes as they have recently been called, were discovered in 1882 by Bizzozero, our knowledge of these, the smallest of the corpuscular
Pl. 10, Fig. 1 constituents of the blood, is still extraordinarily scanty. We do not know with certainty
Pl. 11, Figs. 1, 17 their number or their origin; whether they are cells or not; what their form may be in the circulating blood; nor do we even know exactly how large they are. Their extreme delicacy causes them to perish in large numbers during the act of obtaining a drop of blood no matter how carefully it is performed.

Beyond question the blood platelets are smaller than the erythrocytes, smaller even than the smallest of colorless blood cells. Usually they measure 2—3 μ, rarely somewhat more; their form is irregular and apparently variable as well, for it is possible they have power of amoeboid movement although it is disputed. The fundamental form of the platelets seems to be that of a flattened sphere or ellipsoid, yet highly irregular forms are observed, with pointed processes etc. These processes have been called pseudopodia but many consider them to be non-motile projections of the cell. Examined in the fresh condition the platelets appear quite colorless and without recognizable structure. Their number is usually given as 300,000 per cmm. but recently has been estimated as decidedly higher, even up to 900,000. Although there is some variation in the appearance of the blood platelets in the fixed and stained condition, yet an internal body stained like a nucleus, or a mass of colored granules which are known by the quite unsatisfactory name of "chromomeres" can usually be distinguished from an unstained, homogeneous outer zone, known as the hyalomere. Although it stains with nuclear dyes the nuclear nature of the central mass is denied.

While the blood platelets were originally considered to be involved in the process of the clotting of blood, whence the name thrombocytes, and although this view is still accepted to-day in many different quarters, yet there are investigators who take exactly the opposite view. The question of the origin of the blood platelets is just as undecided. Some consider them to be cells, others explain them as albuminous precipitates (!); the most probable idea of their nature advanced up to the present is that they are fragments of megakaryocytes (p. 93). In any case they are extremely perishable structures which in drops of blood outside the body disintegrate in spite of all precautionary measures. Usually just before their final disappearance they are seen to assemble in small groups.

Blood Dust, Haemoconia

While the cellular nature of the blood platelets is questionable there is no doubt that the fine "dustlike" particles which circulate in the blood are of a non-cellular nature. The large majority of them are extremely fine droplets of neutral fat, the rest are perhaps of albuminous materials. The amount of this blood dust depends upon the amount of nourishment and the time since it was absorbed. As the name indicates the size of the particles is very small, less than 1 μ.

Appendix: The Cells of the Red Bone Marrow

Although in the embryo erythrocytes are formed in both liver and spleen, in the adult body the red bone marrow (p. 134) is the only site where the red blood corpuscles are produced. Because of the brief life of these corpuscles constant reinforcement of their numbers is necessary. In the red bone marrow are found the nucleated antecedents of the erythrocytes and in addition granular leucocytes are also formed there. Pl. 11, Figs. 18–20

In the fundamentals of its structure red bone marrow is closely related to organs formed of adeno-lymphatic tissue inasmuch as its cellular elements lie in the meshes of a syncytium consisting largely of reticular connective tissue. Within the marrow are found sinusoidal venous capillaries with walls of very primitive type (p. 148). Throughout the reticulum and between the vessels lies the myeloid parenchyma proper composed essentially of two types of cells, myelocytes and erythroblasts, the latter being the cells from which the erythrocytes are derived.

The **erythroblasts** are spherical, nucleated cells of the parenchyma of the bone marrow, which usually lie close together in groups. They have spherical nuclei, rather rich in chromatin, while the cytoplasm is more or less yellowish because of its content of haemoglobin; otherwise it appears almost homogeneous. Most of the erythroblasts correspond closely in size to erythrocytes and are aptly termed normoblasts; while a much smaller number of rather larger size are known as megaloblasts, and are apparently the antecedents of the megalocytes (p. 83). The ordinary erythroblasts are somewhat larger than erythrocytes and what is even more characteristic contain less haemoglobin. They increase by mitotic division; the somewhat smaller daughter-cells then develop decidedly more haemoglobin and their nuclei become smaller and more rich in chromatin; they are now the normoblasts proper of histological literature. Pl. 11, Fig. 20

The erythroblast, like the normoblast, is distinguished from the completed erythrocyte of the circulating blood by the possession of a nucleus and by the further fact that it has not yet assumed the disc-like form of the red blood corpuscle but is an approximately spherical cell. The transformation into the definite erythrocyte thus has as a prime necessity the LOSS OF ITS NUCLEUS by the erythroblast. The preparations for this process are clearly seen in the nucleus itself as it becomes pycnotic, its staining is uniformly dark, it becomes smaller in volume and its surface is marked by irregular lumps. As to just how the cell rids itself of this pycnotic nucleus there are two views. The one considers that the remains of the nucleus dissolve intracellularly, although no part of this process has been directly observed. According to the other view which rests upon certain actual observations the pycnotic nuclear remnant is extruded from the cell. Probably then, in this latter manner, the erythrocytes are formed from the erythroblasts; from the parenchyma they reach the sinusoids of the marrow and so enter the blood stream. Rarely is an erythroblast with pycnotic nucleus to be found in the circulating blood.

Pl.11, Fig.20 The descendents of the cells of the primary bone marrow of the embryo (p.137) constitute the bulk of the cellular elements of the red bone marrow and include the cells from which the granulocytes are derived. Two varieties of these latter cells may be distinguished; those of the one variety are usually termed myeloblasts because they represent the mother cells of the distinctive marrow cells or myelocytes. The other variety is that of the myelocytes themselves. In some quarters the cells of the first variety are considered to give rise to both myelocytes and to erythroblasts and are termed haemocytoblasts. They are non-granular lymphoid cells while the myelocytes are granular and already show all the three types of specific granulation (p. 89). The myeloblasts (haemocytoblasts) are relatively large cells, 10—15 μ in diameter, and have basophilic protoplasm surrounding a relatively large nucleus which usually occupies a somewhat eccentric position. Apparently they have power of amoeboid movement. They occur singly or in small groups, never in masses, and resemble lymphoblasts, the stem-cells of the lymphocytes as found in the germinal centers of lymph glands etc.

The **myelocytes** arise as granular daughter cells through the division of these myeloblasts. Just as in the granulocytes of the circulating blood there may here be distinguished three varieties of myelocytes according to their type of granulation, neutrophilic (or better special), eosinophilic, and basophilic myelocytes. The granulations of the myelocytes show no essential differences from those of the cells of the circulating blood. On the other hand the nuclei are not as yet polymorphous like those of the blood cells but are compact although often reniform. For the myelocytes in contrast to the polymorphonuclear leucocytes are capable of cell division; they increase through mitosis and their daughter cells then assume the character of the leucocytes of the circulating blood. In this latter process the originally compact nuclei of the daughter cells become deeply constricted. Only in one regard does there still exist a difference, viz. in the proportionate numbers of the various kinds of myelocytes. As in the circulating blood the special type of granulation is most common, but among the myelocytes its preponderance is not so great; in particular the eosinophilic granulation is markedly more frequent than in the circulating blood. Many authors explain this difference by assuming that the eosinophilic granulation of myelocytes is of a different kind from that of the blood corpuscles. In a certain sense a like difference in proportion obtains also for the basophile myelocytes; it is true that again they are the least common in occurrence but their frequency in the marrow stands in no relation whatever to their extremely small numbers in the circulating blood.

Beside true lymphocytes which are by no means lacking in the marrow, another type of cell is found which, in man and under normal conditions, occurs solely in the red bone Pl.11, Figs.18, 19 marrow. These cells are the **megakaryocytes**, a variety of giant cell with but one nucleus and consequently not to be confused with such polykaryocytes as the osteoclasts (p. 15). They are large spherical cells 40—50 μ in diameter with peculiarly polymorphous massive, nuclei. The nucleus displays an extraordinary number of rounded masses and usually contains in its interior a cavity which naturally is filled with cytoplasm; for the wall of the cavity is not complete, thus there is direct connection between the intranuclear and the circumnuclear cytoplasm. The result is that in sections through the cell the picture usually Pl.11, Fig.19 seen is that of a ring-nucleus. No matter how polymorphous the nucleus may be it still is a single mass; megakaryocytes are thus never bi- or multi-nucleate. The great size and strongly polymorphous character of the nucleus of these giant cells of the bone marrow result from pluripolar mitoses that may be seen when the cells are as yet smaller and indifferent. The result of these mitoses is always an incomplete division of the nucleus while division of the cell never occurs. The more frequently these mitoses succeed one another the larger and more polymorphous does the nucleus become. Connected with the foregoing is the fact that there is always found in a megakaryocyte a large, often a very large, number of centrosomes which originate in the repeated processes of division.

Since the giant cells of the bone marrow also belong to the great family of colorless blood cells they show amoeboid movement; phagocytosis has also been observed in them. Indeed an occasional leucocyte is met within their cytoplasm; however it is an open question whether the leucocyte has actively penetrated the giant cell by virtue of its own amoeboid movement or whether it has been passively phagocytosed. The giant cells also push processes into the venous sinuses of the marrow; the processes then become abstricted and form the blood platelets. Whether the entire cell ends by becoming subdivided into platelets is uncertain. Megakaryocytes are cells of unstable nature; probably they have no great duration of life. In the embryo they are found in localities such as liver and spleen where the embryonic blood is being formed.

Appendix II: Endothelium

The last member of the great group of the supporting and connective tissues, endothelium, must now be considered. The cells of the connective tissues are well understood Pl.8, Figs.5–7 to be descended from those of the embryonic mesenchyme, never from those of the germ Pl.23, Fig.5 layers which are arranged after the fashion of a simple stratified epithelium. But since the Pl.24, Figs.4, 6 cells of endothelium have exactly this arrangement endothelium is not to be classified on Pl.78, Fig.2 the basis of its structure. The place of endothelium among the connective tissues is shown first of all by its undoubted origin from cells of the connective-tissue — mesenchyme group, and secondly by the fact that in many places it passes directly and with perfect continuity into true connective tissue, for instance into reticular connective tissue.

Endothelium lines many cavities which are derived from clefts in the embryonic connective tissue, such as those of the heart, and of the blood and lymphatic vessels, the anterior chamber of the eye, the articular cavities, bursae etc. Frequently the endothelial covering of the inner surface of such cavities is by no means complete, not even in the case of the vascular system the cavities of which show the most complete form of endothelial lining. The serous cavities (p. 34) on the other hand are not lined by endothelium but by epithelium.

In its most perfect form endothelium consists of extremely flat cells with correspondingly flat nuclei and more or less regularly hexagonal form, placed side by side like an epithelium and united by a true intercellular cement which may be blackened by solution of silver nitrate (p. 30). Under certain circumstances such an endothelium may be in no way different morphologically from an epithelium. For in the latter case also the cell boundaries often are not straight but, as is often the case in very marked degree with endothelium, wavy or even zigzag. Inspection of such an endothelium will not serve to determine that it is not an epithelium; that can be done only by demonstrating its connective-tissue origin and its direct continuity with true connective tissue; things which are out of the question for an epithelium. Endothelium always occurs as a single layer of squamous cells, never in a stratified form.

Although it does not fall within the province of this book either to cite authors or to touch upon disputed points, yet in view of the great obscurity which surrounds the term ENDOTHELIUM and its distinction from epithelium, the point of view adopted in this book must be briefly explained. The general understanding of the term endothelium has already been accurately summarized above; and if the definition there given were adhered to there would be no doubt as to what should be termed endothelium and what epithelium. However some authors apply the term endothelium to structures which according to the above definition are undoubtedly epithelia; while many others reject the term endothelium altogether. The term was indeed introduced at a time when the relations in question were not clearly understood.

The following two detailed examples are offered in explanation. A typical endothelium, one which in places is extraordinarily like an epithelium is that of the anterior chamber of the eye. It lies upon the posterior surface of the cornea (p. 262) with such regularity of form as to simulate a typical simple squamous epithelium; indeed it is not at all to be distinguished from such. But the anterior chamber of the eye is formed relatively late as a cleft in the embryonic connective tissue; the epithelial part of the anlage of the eyeball does not in the least enter into its formation. Consequently the lining of the cavity, notwithstanding its epithelial appearance, can be formed only from connective-tissue cells. Moreover the resemblance of the lining of the anterior chamber to an epithelium becomes less the more nearly it approaches the angle and posterior wall of the chamber; on the anterior surface of the iris, which forms the posterior wall of the cavity, the resemblance is very slight indeed, the endothelial cells passing gradually and with complete continuity into ordinary connective-tissue cells. By definition this is a characteristic of endothelium and is found also in very pronounced form in other places (see reticulo-endothelium below). If what is here called endothelium is given the name of epithelium then logically no objection can be raised to calling every connective-tissue cell an epithelial cell.

Others while recognizing the concept of an endothelium extend it to cover the epithelium of the serous membranes, solely upon the ground that in certain places — particularly the thinner portions of the great omentum (p. 220) — this epithelium is extremely thin and flat. But, in the first place, the epithelium of the serous membranes is formed from the epithelial lamellae of the lateral plates of the embryo, from which, in a similar manner, undoubtedly epithelial structures take their origin. In the second place it is indeed true that in adults the serous epithelium frequently consists of a very flat, almost endothelial-like covering; however this is not so in the embryonic condition. For in the embryo the caelomic epithelium is columnar, or at least cubical, for a long time; it may also bear epithelial differentiations such as cuticular or even ciliary borders, things never found on endothelia. Moreover even in adults this epithelium, *e. g.* in the peritoneum, passes more than once directly from the greatly flattened condition into a low cubical variety; and at the border of the ovary it (the "endothelium" of many authors!) is continued as the truly columnar germinal epithelium from which the female sexual cells, the ova, are formed. Thus if the epithelium of the serous membranes is to be called endothelium in spite of its undoubtedly epithelial origin in the embryo, no fault is to be found if the ova or sperms are explained as endothelial cells. On the same basis another conclusion might be drawn, viz. endothelium is derived from ciliated epithelium; embryonic ciliated epithelium becomes transformed into endothelium!! Others disregarding facts and consistency have used the term "mesothelium" for the serous epithelium. This is but adding a name, it is not a step toward settling the confusion which in many ways prevails upon this point.

Endothelium always appears as a flat, and usually extremely thin, cellular coating; but it is not always exactly the same, its appearance varying from that of sharply bounded cells connected by cement to that of a true syncytium. One place in the human body

Pl.8, Figs.5, 6
Pl.78, Fig.2

where endothelium assumes a particularly regular form, and hence appears exceedingly like an epithelium, is the posterior surface of the cornea. In this situation the endothelial cells not only have sharp and even boundaries but they are not even extremely flat, the nucleus producing only a slight bulging of the surface of the cell. In many animals the nucleus is kidney-shaped with a centrosome lying in the depression. With certain exceptions (to be dealt with just below) the endothelium of the vascular system in general is similar; only in this case the endothelial cells are decidedly flatter and their boundaries markedly wavy. In form the cells are always elongated, their long axes being parallel to that of the vessel. The more the latter is stretched the less wavy do the cell boundaries Pl.8, Fig.7 appear. The cement between the cells must be very soft since it permits the passage of colorless blood corpuscles. The nucleus, although flattened, produces a distinct convexity on the surface of the cell.

In certain situations in the body the structure of the vascular endothelium changes to the extent that cell boundaries are lacking, *i. e.* it is present as a syncytium. This is notably the case in the capillaries of the liver, the endothelial relations of which will be discussed below. In the capillaries of the chorioid coat of the eyeball (the membrana choriocapillaris) the endothelium is syncytial, also in the capillary loops of the renal glomeruli; in a certain sense also in the splenic sinuses and the sinusoidal (venous) capillaries of the Pl.53, Fig.4 red bone marrow. But above all, the endothelium of the lymph sinuses in the lymph glands shows peculiarities, inasmuch as it passes without any sharp boundary into the syncytium of the reticular tissue; where endothelial cells cease and reticular tissue begins cannot be at all determined.

In the endothelial cells of the sinuses within the lymph glands and in certain cells of the capillary walls in the hepatic lobules, the so-called stellate cells (p. 216), an important physiological function, namely that of phagocytosis can be observed. Endothelial cells are not only of connective-tissue origin but like the cells of reticular tissue still exhibit primitive characteristics, such as phagocytosis, which have been lost by the more highly differentiated cells of connective tissue. Thus in lymph glands the endothelial cells of the lymph sinuses take up by phagocytosis foreign bodies which have been brought to them in the lymph; moreover they may themselves become detached and enter the lymph stream. This power of phagocytosis is present to a most marked degree in the so-called stellate cells of the capillaries of the liver which represent endothelial cells specially modified for purposes of phagocytosis; and which, in contrast to the endothelial syncytium of the same region, play a somewhat independent role.

The fact that in many places endothelium has a syncytial arrangement is not at all to be regarded as a more advanced differentiation. On the contrary such endothelial conditions, and in the walls of the splenic sinuses they occur in particularly primitive form (p. 154), must be regarded as a less differentiated type of vascular endothelium.

As already mentioned endothelial cells are not only connective-tissue elements but represent relatively primitive types of such elements. Thus their nuclei have a striking resemblance to those of fibrocytes, to which the endothelial cells are related in the sense that both varieties of cells are direct descendents of the embryonic mesenchyme. But of all the relationships of endothelial cells the closest is to reticular tissue; and this topic leads to a short digression into a much disputed subject, viz. that of the RETICULO-ENDOTHELIUM. Recently even a "reticulo-endothelial system" is spoken of; the term system not being used in its ordinary sense in anatomical nomenclature but largely with physiological implications. Beyond doubt it is more easy to outline the conception physiologically than along strictly morphological lines. This more or less complete removal from the field of normal anatomy goes so far that the right of the conception to existence has been absolutely denied. Naturally only the morphology of the reticulo-endothelial system may be discussed here and the points still in dispute will be almost neglected.

THE RETICULO-ENDOTHELIAL SYSTEM

Under this name there are grouped first of all the syncytial arrangement of reticulum cells in the splenic pulp, in both the cortical nodules and medullary cords of the lymph glands (p.149) and in adenoid tissue elsewhere (p. 72); also the reticulo-endothelia proper, *i. e.* the transitional forms between endothelial cells and syncytial reticulum elements such as the cells of the walls of the sinuses in lymph glands etc. (p.151). In addition the endothelial cells of the splenic sinuses and of the hepatic capillaries, particularly the stellate cells, are considered to belong to the reticulo-endothelial system; also the endothelial cells of the red bone marrow, adrenal gland, and hypophysis.

The prime requisite for the inclusion of the above cells in a compact group is the common characteristic that they take up with great intensity dyes which other connective-tissue cells reject entirely or in great measure. On this ground the histiocytes, which also take up dyes (p. 55), the myelocytes (p. 155), and the monocytes among blood cells, belong to the reticulo-endothelial system in the wider sense. The idea of the genetic connection of these cells is based upon viewing the monocytes of the blood as derived from the histiocytes or from the reticulo-endothelium. The cells of the latter have consequently been termed histioblasts; and histiocytes, myelocytes and the blood mono-(histio-)cytes are together termed the histiocytic elements among connective-tissue cells. This would recognize a special place among the colorless blood cells for the so-called monocytes. They must then be considered true reticulo-endothelial cells, or myelocytes, or histiocytes which have become motile and passed into the blood.

Considering the purpose of this book, and the space available, as well as the lack of unanimity as to the relations of the blood cells to one another and to the cellular elements of the connective tissue, the presentation of the subject must be limited to this brief sketch.

Muscular Tissue

The designation "muscular tissue" is really derived from the physiological function of its elements. Under this name are included those histological elements which produce muscular movement. This variety of movement in animal tissues differs essentially from amoeboid and ciliary movement in being evoked through the influence of the nervous system, indeed under normal conditions through this influence alone.

The cellular elements of muscular tissue are termed FIBERS (often incorrectly) and are of varied forms; but they all contain fibrils which are to be considered the true contractile structures, a conclusion justified on many grounds. Beyond these common characteristics of muscle fibers there are very important histological differences and frequently a quite different histogenetic source as well. As a result, in vertebrates and consequently in man, three varieties of muscular tissue may be distinguished: 1. smooth muscle; 2. striated muscle; 3. cardiac muscle. Of these the simplest form is

1. Smooth[1] Muscle

The elements of smooth muscle are simple contractile cells (muscle cells). Their form
Pl.12, Figs.1–3 is that of an elongated spindle with sharply pointed ends which occasionally are bifurcated.
They do not properly deserve the term "fiber" which has long been applied to them, not
Pl.13, Figs.1, 2 even when, as is occasionally the case, the cells are not exactly spindle-shaped but are
somewhat flattened and strapshaped. The cells of smooth muscle are thus thickest in the

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[1] Concerning this term see footnote, p. 97.

middle of their length and become progressively narrower from that region to their ends. The nucleus, and there is never more than one, is elongated and is to be found where the cell is thickest. It has a distinct nuclear framework and nucleoli; its form, and especially its length, varies as does the length of the cell itself, although not exactly to the same degree.

The length of smooth muscle fibers is variable within quite wide limits; however the variations in length are trifling compared to those of striated muscle (p. 99). Usually the fibers are between 30 μ and 250 μ in length, although in the walls of many blood vessels there occur still shorter fibers, and in the muscle of the pregnant uterus fibers which are much longer. Fibers may be considered of average length when between 50 and 150 μ. In long fibers the nucleus is almost rod-shaped and occasionally twisted into a spiral form. Its length is 15—20 μ but the thickness only 2—3 μ. Very short fibers are usually relatively thick and have nuclei in the form of short ellipsoids. The greatest thickness of the smooth muscle fiber is determined by the nucleus and consequently is but slight, a sharp contrast to the length of the fiber; on an average it varies between 5 and 10 μ. The fact that only the middle part of a smooth muscle cell contains a nucleus, determines (Pl.13, Fig.1) that in a cross-section of smooth muscle but few nuclei are seen; and that in general the more or less circular cross-sections of the fibers present both large and small areas, the smallest being the pointed ends of the fibers cut across. Many muscle fibers of the walls of arteries, especially of the larger arteries, show a variation from the form just described. They are short, broad, and usually flattened cells whose ends are deeply forked, or even more extensively branched.

Pl.13, Fig.2

In suitable preparations the protoplasm of smooth muscle cells usually appears finely striated[1] for it contains the contractile fibrils (myofibrils). These are structureless and anisotropic throughout their whole length. They lie in the long axis of the cell, and being few in number, and not grouped but evenly distributed in the protoplasm, are considerable distances apart. Occasionally there are indications of arrangement in bundles and uneven distribution in the protoplasm. The smooth muscle cells of many rodents contain fibrils which are few in number but are unusually stout; possibly they are tonofibrils. The thickness of myofibrils appears to vary within considerable limits, from 0.2—4 μ; naturally in cross-section they appear as points. Often in cross-sections of smooth muscle only a varying proportion of the fibers present show distinctly the dots representing the myofibrils; the remaining fibers then usually appear much darker and more homogeneous. A cell membrane is lacking in smooth muscle fibers; but there is a somewhat denser, external layer (Pl.13, Fig,1) which, however, is not always free from fibrils. The protoplasm shows, as a rule, no other structures; although around the nucleus there are often small granular inclusions, lipoid granules. It stains relatively easily with acid aniline dyes such as eosin, and then usually takes a decidedly darker tint than the surrounding collagenous connective tissue. Other methods also stain the plasma of smooth muscle cells, some of them in a quite selective manner; solution of palladium chloride stains it yellow.

Smooth muscle is widely distributed in the human body particularly as the muscle of the viscera. It is a variety of muscle which without exception (?) is beyond the control of the will and is innervated by the sympathetic nervous system. Smooth muscle is found in the wall of the digestive tract for almost its entire length, in the wall of the respiratory tract and its branches, in that of the genito-urinary tract (ureter, bladder, urethra, epididymis, ductus deferens, seminal vesicle, prostate; oviduct, uterus, vagina); in smaller quantity in other viscera (ducts of glands, spleen); in the intrinsic muscles of the human eye and the small muscles of the hairs of the skin (mus. arrectores pilorum), and occasionally in other smooth muscles of the skin not connected with hairs (p. 303). The musculature of the vascular system, with the exception of the heart, is of the smooth variety.

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[1] Often in stained preparations, and also in cells which have been isolated, this striation is not seen. The muscle fiber then appears "smooth" *i. e.* not striated; hence this much used, but rather unfortunate, term.

In contrast to the two tissues (epithelium and connective tissue) already treated, smooth muscle, and muscular tissue in general, shares with nervous tissue (although in a certain sense differently, see below) the peculiarity that its structural elements are not capable of forming a mass of tissue of themselves alone. For like glands, in which the epithelial tissue requires the presence of connective tissue, muscular tissue for its nourishment must be combined with connective tissue, be the latter ever so small in amount. In other words smooth muscle, and muscular tissue in general, never show that direct contact of structural elements which characterizes epithelial tissue and is also the case with the fibrocytes of connective tissue.

Although the separate cells of smooth muscle lie so close together that it was long assumed they were united by a cement substance, actually a certain amount of connective tissue intervenes between the adjacent cells. Smooth muscle fibers, either singly or in small groups, are rarely found detached and bare in connective tissue; although this is the case in the intestinal villi and in a few other mucous membranes, and in networks of single
Pl. 47, Fig. 2 fibers and of small groups as in the bladder of the frog. Usually smooth muscle with its
Pl. 40, Figs. 2, 3 related connective tissue occurs in compact formation as in the so-called coats, the tunicae musculares, of the intestinal wall etc., or in layers of considerable thickness such as the heavy muscular wall of the uterus, or as a mass of muscle filled with glands such as the prostate. In formations like these the individual smooth muscle cells lie close together, and as may easily be understood the thick part of one cell containing the nucleus lies opposite the thin ends of neighboring cells. Consequently in sections of smooth muscle the nucleated middles of fibers alternate with the non-nucleated ends; this is seen most clearly when the section cuts the fibers longitudinally. Only rarely, and in small smooth muscles such as the mus. arrectores pilorum, do the middle portions of the fibers with the nuclei lie side by side, producing an appearance of many nuclei in a row and causing a considerable thickening of the muscle in that region.

As regards the manner in which the fibers are held together, it has already been mentioned that in spite of the first impression that each cell is in direct contact with its
Pl. 13, Fig. 1 neighbors yet connective tissue, reduced to the least amount possible, is present between them. The name **MEMBRANELLAE** has been given to these extremely delicate, non-nucleated membranes of connective tissue, which lying between the separate fibers hold them all quite firmly together. It is these membranellae which prevent isolation of the individual muscle cells unless a reagent, such as caustic potash, has first been employed. Such reagents dissolve the membranellae and make isolation of the cells comparatively easy. It is very doubtful whether these delicate sheaths of the smooth muscle fibers consist of collagenous connective tissue; it is much more certain that reticulum fibers are present in them. However the membranellae are connected with the stouter strands of true collagenous connective tissue which carry also elastic fibers, vessels and nerves, and separate the
Pl. 77, Fig. 2 bundles of smooth muscle fibers. Many smooth muscles, *e. g.* the ciliary muscle of the eye, contain such connective tissue in large amount and are broken up by it into numerous small bundles; and elsewhere, *e. g.* in the muscular wall of the ureter, there occur small

bundles sharply separated by connective tissue. On the other hand the two layers of muscle in the intestinal wall consist of compact masses of smooth muscle cells; it is only between the layers that there is found a coarser sheet of true collagenous connective tissue.

Small smooth muscles, such as those of the skin, terminate in tendons just as do the skeletal muscles formed of the striated variety; however these tendons are very short and slender and usually consist of elastic, not of collagenous, fibers.

The membranellae through an artefact may simulate intercellular bridges between smooth muscle cells and were once commonly accepted as such. Transverse folds form very easily in these delicate membranes if the enclosed muscle cells shrink, thus producing an indistinct impression of delicate processes Pl. 13, Fig. 2 joining the muscle cells together. In reality the apparent processes are merely folds of the membranellae crossing the intervals between neighboring fibers, intervals which have been artificially widened by shrinkage of the fibers. Naturally the most delicate branches of the (non-medullated) nerves supplying the smooth muscle fibers run in the membranellae.

Smooth muscle in man and vertebrates is almost without exception a product of the embryonic mesenchyme; consequently it is from the same source as the embryonic connective tissue. In exceptional cases (a portion of the intrinsic muscle of the eyeball and the coiled sweat glands) it is derived from the outer germ layer and is thus of epithelial origin, its cells being known as myo-epithelial cells (p. 38). The sweat glands show with especial distinctness that although these epithelial muscle cells agree perfectly in structure with the true smooth muscle cells of mesodermal-mesenchymatous origin, they still display many primitive characteristics. Thus, as may easily be understood they dispense with membranellae since they lie internal to the membrana propria; neither do the individual muscle cells lie close together as in typical smooth muscle, but are distinctly separated by vacant intervals. They also pass without interruption into ordinary epithelial cells. In this category belong also the so-called basket cells of many glands (p. 51).

2. Striated Muscle

Pl. 12, Figs. 4—8
Pl. 13, Figs. 3—9

Although occasionally the elements of striated muscle are mingled with those of smooth muscle for the performance of the same function, yet in their structure as well as in their comparative size the two varieties differ most widely. Muscular movement can thus be produced through two types of contractile elements which are totally different from one another. While in general a physiological difference in function is demonstrable between the two chief types of muscle yet they can act together in harmony, as for example in a large part of the wall of the oesophagus and in other localities.

The outstanding feature of striated muscle is that the elements are not simple, uninuclear structures which have the value of single cells, but are multinucleate syncytia (plasmodia). Striated muscle is by far the more highly differentiated type of tissue. It forms all the skeletal muscles without exception, and in part those of the viscera (see below). The fibers have essentially a cylindrical form.

The fiber of striated muscle always exceeds the cell of smooth muscle in size and usually to an enormous degree and in every dimension, but particularly in length; for the length of the fiber is largely independent of that of the muscle to which it belongs. If a muscle is rather short the fibers run from one end to the other; but long muscles have long fibers, particularly if the length of the muscle is greater than that of the fibers. Thus the fibers of striated muscle may be 12 cm. long and occasionally, as in the human musculus sartorius, even longer. The extreme measurements for the length of fibers of human striated muscle are said to be from about $\frac{1}{2}$ to 12 or 15 centimeters.

The variation in DIAMETER of fibers of striated muscle, although less than that of their length, is yet quite considerable, the thinnest fibers measuring scarcely 10 μ, the thickest almost 100 μ. Thus in proportion to their length, which in some cases is very great, the fibers of striated muscle are relatively thin and the name "muscle fiber" is much more appropriate than it is for the spindle-shaped cells of smooth muscle. The thickness of striated fibers is in no way dependent upon their length, long fibers may be relatively slender. However physiological function seems to have a relation to the thickness of fibers to the extent that muscles which perform the finer types of work usually have thinner fibers than those which are involved in rougher work. The thickness and the length of fibers are dependent upon the condition of the muscle as regards contraction; for not only is the muscle as a whole shortened in contraction but each individual fiber shortens and becomes thicker.

The form of the fiber of striated muscle, unless altered by some external influence, is that of a true cylinder. The striated muscle fiber of man, and of most animals as far as they possess this type of muscle, has the form of a cylindrical cord, usually quite long and of varying thickness (20—50 μ). Only the ends of the fibers show more or less departure from the cylindrical form. Two different types of ends may be distinguished: first, ends which connect with tendons (and almost all muscles possessing striated fibers terminate in tendons); second, intramuscular ends. If the fibers run throughout the entire length of the muscle both ends of the fiber will be "tendon-ends". But if the muscle is longer than its fibers, thers will be found within it two fibers fastened together (see below) one of which continues the direction of the other. These fibers may show either one tendon-end and one intramuscular end; or, infrequently, two ends of the latter type. The difference between these two types of endings is very slight. The tendon-ends are somewhat tapered, but this is not the case with the intramuscular ends. The termination of the former may be either rounded, hemispherical or oblique. Oblique endings are common if the tendon does not continue in the axis of the muscle. Almost without exception the intramuscular ends are oblique; in this case the oblique ends of the two fibers, which are joined to one another, fit together exactly.

Only in rare cases are the fibers of striated muscle branched at one end. This appear-
Pl. 12, Fig. 8 ance is almost confined to the striated muscle of the tongue and in man never reaches such an extreme degree as it does in very mobile tongues, *e. g.* that of the frog. Never more than a certain proportion of the muscle fibers are thus branched. Striated fibers with branched ends occur in the superficial muscles of the face, but less frequently than in the tongue.

In the fresh condition the fiber of striated muscle is a soft structure of very high plasticity, so that external influences can alter decidedly the form of the fiber. The unavoid-
Pl. 12, Fig. 7 able shrinkage of tissues, and particularly of muscular tissue, during fixation causes the
Pl. 27, Fig. 2 close-set cylindrical fibers to be slightly flattened. In cross section then, instead of being rounded the pictures of the fibers are polygonal.

The occurrence of striated muscle in man is very extensive. Without exception it forms the skeletal musculature as a whole and the muscles of the tongue, larynx, and pharynx, and the muscle of the upper part of the oesophagus. Also the extrinsic muscles of the eye, the superficial muscles of the face, including the muscles of the ear, the muscles of the middle ear, the perineal and anal muscles and those of the external genitalia; all these consist of striated fibers which, however, occasionally occur along with those of smooth muscle.

Striated muscle is much better adapted to examination in the fresh condition than is smooth muscle since its fibers, unlike those of the latter, may easily be isolated; their greater size is naturally also an aid. When the fibers are viewed under the microscope in indifferent media, such as physiological salt solution or Ringer's solution, even moderate magnification reveals the TRANSVERSE STRIATION which has given its name to these structures. At least it is the rule that these structural elements of muscular tissue should appear striated; but occasionally the striation is completely lacking or it is indistinct, and in its place a more or less marked longitudinal striation is recognized, either alone, or along with an indistinct cross striation. The striated muscle fiber deserves this name only to the extent that under the microscope cross striation as described is, as a rule, its most noticeable feature. This appearance, which primarily is an optical phenomenon and is indicative of the structure of the fiber to only a limited degree, may be absent. So-called (transversely) striated muscle fibers may thus appear under the microscope more or less distinctly striated longitudinally. The latter picture, far more truly than that of the transverse striation, corresponds to the histological structure of the fiber. Pl. 12, Fig. 4 Pl. 13, Figs. 3, 8

As a rule, there may be recognized in the fibers of striated muscle transverse lines, alternately light and dark, and at exactly even intervals. These lines run through the whole thickness of the fiber from one margin to the other. The pale lines or bands are singly refractive (isotropic); the dark bands are double refractive (anisotropic) and cause the light to become positively polarized. This picture may be followed through the whole length of the fiber and usually with striking distinctness. Nevertheless, as we shall see from the true structure of the muscle-fiber syncytium, this appearance does not justify the assumption that the fiber of striated muscle is composed of alternating isotropic and anisotropic discs. However as often happens for the sake of a simplified nomenclature the term disc is used; but it must be borne in mind that this name rests upon an optical illusion. If, in many human striated muscle fibers, the pale, isotropic transverse band is examined closely under even moderate magnification it is seen to be divided evenly into two bands by a fine line which is dark and consequently is anisotropic. This line has been named the INTERMEDIATE LINE of Krause after its discoverer, or more briefly the Z-line or Z-striation (or telophragma). Usually it is still more difficult to detect the LINE OF HENSEN (M-line or mesophragma) which is a pale, isotropic line dividing in a similar fashion the principal dark, anisotropic band. However, under high magnification it is usually demonstrable without difficulty in human muscle fibers after death. All these appearances in the microscopic pictures of fresh fibers find their explanation when the more minute structure of the striated muscle fiber is considered. Pl. 12, Fig. 4 Pl. 13. Fig. 3 Fig. 13

The fiber of striated muscle has already been characterized as a multinucleate plasmodium or syncytium; that is to say it consists of a mass of protoplasm in which are situated a large number of nuclei. The protoplasm of muscle fibers has long been known as SARCOPLASM, a special term which really is superfluous. Even in smooth muscle the sarcoplasm is not to be regarded as the contractile substance. The latter is represented even more obviously in the fibers of striated muscle by the fibrillae (myofibrillae), which thus form the third chief constituent of such fibers. In addition the muscle-fiber syncytium has as sheath a membrane which has long borne the name of SARCOLEMMA. Thus the fiber of striated muscle is made up of four chief constituents 1. sarcoplasm, 2. nuclei, 3. myofibrils, 4. sarcolemma. The latter appears to be a kind of cell membrane but is not really such (see below). The fibrils are, as always (p. 8), differentiations of the protoplasm. In the fully developed striated fibers of man the number of fibrils is extraordinarily great, so much so, that in bulk the remaining constituents form much the smaller mass. It is a fair estimate that, as a rule, more than nine tenths of the substance of a striated fiber is formed by the fibrils. Of all the constituents of the fiber only the fibrils are "striated", that is consist essentially of alternating isotropic and anisotropic substances (p. 102). All the fibrils have the same arrangement within the fiber, *i. e.* a transverse plane of the fiber contains either all isotropic or all anisotropic segments of fibrils. This fact along with the great bulk of the fibrils determines the apparent composition of the fiber as a whole from alternating singly and doubly refractive elements. In other words it determines the picture of the striation; which is all that is usually seen in fibers in the fresh condition, the nuclei being barely indicated.

Since the **fibrils** are differentiations of protoplasm they naturally lie within the protoplasm, or sarcoplasm, of the muscle-fiber syncytium; they are thus surrounded by sarcoplasm even when the latter is present in only minimal quantity, as is commonly the case in human skeletal muscle. The same is naturally also true of the nuclei. The fibrils are as long as is the muscle fiber itself and extend from one end of the fiber to the other. The thickness of the fibrils is difficult to determine and seems to vary even within the same fiber. Indeed, the Pl.13, Figs. 4–6 thickness of the selfsame fibril diminishes as it approaches the junction of the fiber with the tendon. Probably the thickness of the fibril is less than 1 μ. Since the fibrils determine the striation it must be possible to demonstrate in each fibril alternating isotropic and anisotropic segments and the Z and M-lines. Indeed, in very highly developed fibers of striated muscle, as for instance those of beetles, a decidedly more elaborate striation may be recognized.

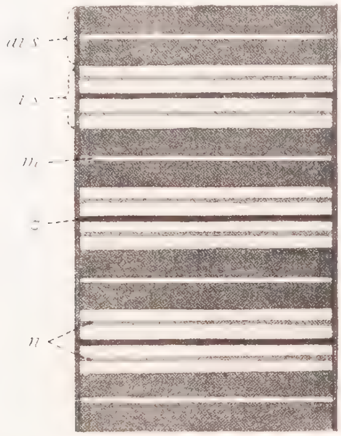

Fig. 13. **Diagram of the Striation of a Muscle Fiber.**

ai s = anisotropic substance
i s = isotropic substance
m = Hensen's line
n = accessory disc
z = intermediate line of Krause

Within the isotropic substance, on each side of the Z-line, there is a dark accessory band. Thus, the isotropic substance is subdivided into two equal parts by the dark Z-line and each of these two parts is again subdivided by the accessory band which, however, is not quite so dark as the Z-line. The significance of this subdivision is not at all clear, indeed it is doubtful if it is a question of preexisting structures at all. After the use of certain reagents the Z-line appears as a transverse membrane running across the masses of fibrils Fig. 13 and connecting with the sarcolemma, which it also resembles in its staining reactions. All these phenomena still need explanation.

By the use of certain reagents the fiber of striated muscle may be broken up into the so-called DISCS OF BOWMAN. These discs may again be resolved into long, slender structures, the so-called sarcous elements, each corresponding in length to the thickness of the disc. In particular the muscle fibers of many beetles may thus be broken up into discs by treatment with 60% alcohol, or with dilute hydrochoric acid. These results are of an entirely artificial nature and depend essentially upon the solution by either alcohol or acid of parts (lines) of the striation as described above.

While the resolution of a fiber of striated muscle into discs is purely artificial, its resolution Pl.12, Fig. 6 into fibrils corresponds to the actual structure of the muscle fiber. However it is not easy to isolate the fibrils completely (for instance by dilute chromic acid); usually a few fibrils will cling together. The striation can be distinctly recognized in even the most delicate parts of the fiber which may be isolated in this manner.

The same picture of the striation, and its subdivisions, is shown in stained preparations of the fibers of striated muscle. The anisotropic substance usually stains the more strongly, the isotropic substance to a much less extent. Thus the anisotropic substance stains strongly with eosin and under regressive methods of staining, such as the iron haematoxylin process, it holds firmly the dark stain which is readily given off by the isotropic substance. This is true not merely for the principal bands but also for their subdivisions.

It has already been noted that the fibrils must lie within the sarcoplasm since they are products of its differentiation. In many muscle fibers, particularly those of most of the skeletal musculature of man, the quantity of fibrils is extraordinarily great; that of the sarcoplasm, on the contrary, is very small, often indeed quite minimal. Consequently the proportion of fibrils to sarcoplasm may vary within wide limits. There are not a few muscle fibers in man which are relatively rich in sarcoplasm (and also are relatively thin) and in which the distribution of the fibrils is uniform throughout the entire area of the sarcoplasm. That is to say, each individual fibril may be seen surrounded by sarcoplasm which separates it from its neighboring fibrils. This condition is usually found in fibers which are rich in sarcoplasm, and it is especially clear in pictures of transverse sections, the fibrils appearing as points distributed at equal distances in the sarcoplasm.

Pl. 13, Figs. 4-6

More frequently a varying number of fibrils, about fifty or more, are arranged in a group. They lie close together, so close that between them there would seem to be no room for sarcoplasm. Such a group of fibrils is termed a MUSCLE COLUMN. The individual muscle columns, the thickness of which varies even within the same muscle fiber, are separated by walls of sarcoplasm of greater or less thickness. When the cross section of such a muscle fiber is examined, areas of irregular shape and varying size may be recognized. These are named COHNHEIM'S AREAS after their discoverer. The richer the muscle fiber in question, is in sarcoplasm the more clearly these areas are seen. This picture which is recognizable in a large proportion of human muscle fibers, still more greatly predominates in those of many animals.

Pl. 12, Fig. 7
Pl. 27, Fig. 2

Cohnheim's areas are scarcely to be recognized in muscle fibers which are poor in sarcoplasm, and such fibers occur in very many human skeletal muscles. In the more extreme of such cases it would seem impossible to find any sarcoplasm at all between the fibrils or the muscle columns. The impression is given that in these cases sarcoplasm is present merely around the nucleus and that within the mass of fibrils it is completely, or almost completely, lacking. The picture of the cross section of such a muscle fiber has a strikingly homogeneous appearance.

When transverse sections of muscle fibers are examined under very high magnification the point-like cross-sections seem so numerous and appear to be so arranged in groups as to give the impression that the individual fibrils are again subdivided into finer elements. The significance of such pictures is disputed.

Views upon the structure of the fibrils are by no means in agreement. While the majority of investigators consider them to be structures of some solidity, either with or without segmentation, it has recently been asserted that they are tubes with fluid contents surrounded by rings formed of the Z-line. According to this conception the cause of the transverse striation lies entirely outside of the fibril and is produced by arrangement of the sarcosomes in rows.

Cohnheim's areas do not stand out so clearly in fresh fibers of striated muscle as they do in those which have been fixed. Even if they are not appearances produced artificially, at least the action of fixing reagents does increase artificially the distinctness with which they may be seen.

The protoplasm of the muscle-fiber syncytium is represented by **sarcoplasm.** An account has already been given of its relation to the fibrils and of the varying quantities in which it occurs. As a rule it appears to have very little structure, only fine lipoid granules being demonstrable within it. These, which have long been known as interstitial granules, are most easily seen in places where the sarcoplasm occurs in larger quantities, *i. e.*

Pl. 12, Fig. 7
Pl. 13, Figs. 3-6, 9

between the muscle columns and around the nucleus. Occasionally they occur in larger numbers, particularly in fibers rich in sarcoplasm, and then produce the so-called DARK fibers; while the fibers which are poor in sarcoplasm and contain few interstitial granules are termed LIGHT fibers. Both light and dark fibers may occur side by side in the same muscle. Naturally these lipoids are dissolved out in making permanent microscopic preparations, certain of the reagents used having the power to dissolve fat; consequently as a rule nothing is to be seen of the interstitial granules in fixed and stained preparations. These granules have well been named SARCOSOMES; they are occasionally arranged ir- Pl.12, Fig 5 regularly but frequently form rows across the fiber. As age increases pigment in the form Pl.13, Figs.4–6, 9 of lipofuscin frequently appears in the sarcoplasm of muscle fibers (p. 16).

The above is based on the assumption that the transverse striation depends entirely upon the relations or structure of the fibrils; but this is disputed. The sarcosomes are often arranged quite transversely and are in a good position in themselves to produce the picture of the transverse striation; moreover fine fibrils join the sarcosomes to one another. It has thus been accepted in many quarters that the fibrils are not segmented but are homogeneous throughout their entire length, and that the striation may be produced through transverse lines of sarcosomes alone. There is also the view that both factors must be considered, segmentation of the fibrils as well as transverse arrangement of the sarcosomes.

Dark fibers, rich in sarcoplasm, occur preferably, and under certain conditions only, in such muscles as must not yield to fatigue but must be able to continue their contractions indefinitely. Beside the muscle of the heart, the principal muscles of this type are the diaphragm, the muscles of the tongue, the extrinsic muscles of the eyeball, and a few others, such as the masseter.

In animals (rabbit, birds) entire muscles frequently consist of fibers all of which are either poor or rich in sarcoplasm, forming either light or dark muscles respectively. These as a rule are distinguishable by their color; muscles with dark fibers are said to be "red", those with light fibers are termed "white". In man such a distinction is not strongly marked. Moreover, the conception of red or white muscles is not exactly the same thing as abundance or scarcity of sarcoplasm. Other factors enther into the question, principally the varying content of haemoglobin which is decidedly greater in red muscles; also the number and position of the nuclei and the relations of the connective tissue within the muscle affect the color of the latter.

It has already been mentioned that fibers of striated muscle occasionally show a distinct longitudinal striation in addition to that which is transverse; indeed there are muscle Pl.13, Fig.3 fibers in which, under the microscope, only the longitudinal striation is visible. Such fibers are always those with abundant sarcoplasm. The longitudinal striation probably does not correspond to the longitudinally arranged fibrils, which would produce too fine a striation, but to the muscle columns. The boundaries of the striae are formed by the septa of sarcoplasm which are particularly distinct when they contain numerous lipoid granules. As may be understood, this interference with the transverse striation blurs the ordinary appearance of the fiber because the fibrils, or the muscle columns which are formed from them, are no longer placed closely side by side and as a consequence of this interruption the individual portions of the striation no longer lie in the same straight line. But chiefly it is the richness of the sarcoplasm in lipoids that makes the picture of the striation indistinct, even to such a degree that occasionally it disappears altogether.

As regards the **nuclei** of the fibers of striated muscle, these occur in numbers which are often quite extraordinary, they may number hundreds and even thousands, depending upon the length of the fiber. In the fibers of human and mammalian muscle in the great Pl.12, Figs. 4, 5, 7, 8 majority of cases they lie close beneath the sarcolemma in a larger or smaller mass of sarcoplasm; so that opposite a nucleus the fibrils do not extend quite to the inner surface Pl.13, Figs. 3, 4, 6 of the sarcolemma. The form of the nuclei varies somewhat; in the first place they are more or less markedly flattened, more in fibers which are poor in sarcoplasm, less in fibers in which sarcoplasm is abundant. The nucleus is always elliptical but the proportion of Pl.12, Figs. 3, 4, 7 its long to its short axis varies. The average limits for the length of the nucleus lie between

8 and 10 μ; the extremes are 5 and 17 μ. The long axis of the nucleus naturally coincides with that of the muscle fiber. The intervals between nuclei are almost exactly the same size. It is only toward the ends of the muscle fibers, especially the tendon-ends, that the nuclei are irregularly distributed and placed more closely together. In these situations also they are frequently in the interior of the fibers. In most muscle fibers a spiral arrangement of the nuclei is distinctly seen. Nuclei are usually much more abundant in thin than in thick muscle fibers.

Although the great majority of the nuclei of muscle fibers lie close beneath the sarcolemma (hypolemmal position) yet, in man, even in adult life there do occur nuclei which lie in the interior of the fiber surrounded by a mass of sarcoplasm. This is the rule in the thin muscle fibers of the muscle spindles (these contain no hypolemmal nuclei, see p. 159) and also at the tendon-ends and in certain muscles, such as the extrinsic muscles of the eyeball. However, in many vertebrates (amphibia, reptiles, fishes, and the white muscle of birds) the nuclei always lie in the interior of the fibers. They may be either central or eccentric but are rarely quite superficial. The same is true of the muscles of many mammals but in man nuclei in such positions are exceptional.

The nuclei of the fibers of striated muscle are scarcely visible in the fresh condition. At most they appear as faint spots; on the other hand they are easily brought to view if the fiber is treated with dilute acetic acid. Naturally they are stained by ordinary basic nuclear dyes, and consequently are readily demonstrated in fixed and stained preparations.

The last constituent of the fiber of striated muscle now to be described is the **sarcolemma.** Pl.12, Fig.7 Pl.13, Figs.3-6, 9 In examination of the fresh muscle fiber it can scarcely be seen so long as the fiber is intact. At most, the facts that a clearly cut marginal contour is visible, and that the soft content of the sarcolemmal tube has a firm consistency indicate the presence of a resistant sheath around the striated muscle fiber. The sarcolemma is most easily recognized if its contents become retracted from it. In such a case there appears a distinct, sharply defined membrane which seems in the fresh condition to be entirely structureless; nor does it show any structure under the ordinary methods of staining. In thickness it approximates 1 μ. It possesses a certain degree of elasticity (?) and like a closed and uninterrupted tube it surrounds the whole length of the muscle fiber, including the ends, whether the latter are intramuscular or are tendon-ends. This tubular form of the sarcolemma is best seen if after the action of reagents the soft contents of the sarcolemmal tube are crushed mechanically so that they are broken up, and short lengths of the empty tube become visible. Under other circumstances the sarcolemma shows not only mechanical powers of resistance but also resistance towards chemical reagents such as acetic acid and weak alkalis.

So homogeneous in its structure does the sarcolemma appear as to suggest a kind of cell membrane enclosing the striated muscle-fiber syncytium. Nevertheless the greater part of its thickness seems not properly to belong to the muscular tissue nor to have been formed by the myoblasts, the embryological antecedents of the fibers of striated muscle. With the aid of certain processes for staining connective tissue (silver impregnation) the greater part of the thickness of the sarcolemma appears to be composed of a close network of delicate reticulum[1] fibers, so that the sarcolemma may well have the value of a connective-tissue basal membrane. Only the innermost layer of the sarcolemma, a very small part of the total thickness of the membrane, appears to belong to the muscle-fiber syncytium itself; yet even for this part such relationship is doubtful. The structure and significance of the sarcolemma are not thoroughly understood. It is noticeable that the Z-line, especially after many staining methods, adheres firmly to the sarcolemma and shows an identical staining reaction.

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[1] The sarcolemma behaves differently in a histo-chemical sense from collagenous tissue. It does not swell in acetic acid nor dissolve in dilute caustic potash, so that while at least the external and chief part of the sarcolemma is of connective-tissue nature it probably is formed of precollagenous reticulum fibers.

To summarize the foregoing: the striated muscle fiber is to be considered as a multinucleate syncytium or plasmodium within which is a variable, and often extremely small, amount of protoplasm, here known as sarcoplasm. In addition there are numberless transversely striated fibrils, forming usually more than nine tenths of the total mass of the fiber, and of themselves determining the transverse striation; usually — but not invariably — they are arranged in bundles (muscle columns). Fibrils, nuclei, and sarcoplasm are surrounded by a tubular sheath, the sarcolemma, which with little doubt is formed of reticulum fibers and consequently does not truly belong to the muscular tissue.

This conception of the structure of the striated muscle fiber is also afforded by its histogenesis and by the basic conditions of the formation of the tissue from cells. Nevertheless other conceptions of the structure of the muscle fibers have been advanced which are essentially further developments of the so-called "muscle compartment" theory of W. KRAUSE. The intermediate membrane (Z-line), first fully described by him, which actually seems to have an intimate connection with the sarcolemma, he considers to be a true membrane running across the mass of fibrils and separating these into compartments. The assumption of M. HEIDENHAIN that the muscle fiber is composed of compartments or inokommata lying one after the other and separated by a membrane, the telophragma, is based upon a corresponding view. The mesophragma then would divide each inokomma through the middle. In some quarters this theory is further elaborated. Concerning the different views upon the structure of the fibrils and the nature of the transverse striation see page 104.

Pl 13, Fig. 7 Another question connected with the histology of striated muscle fiber concerns the relation of the **ends** of the muscle fibers either to those of the tendon into which they are inserted, or to one another, if they are the adjoining intramuscular ends of two fibers which are in direct contact. Formerly, when it was considered that the sarcolemma was a homogeneous, non-connective-tissue membrane, it was assumed that the ends of the muscle fibers were simply cemented together. But now that it can be demonstrated that the sarcolemma, or at least its chief and external part, is a connective-tissue basal membrane, the connection of the fibers may be represented as made through fibrils passing immediately from the sarcolemma of the one fiber to that of the other. In this way the connection between two fibers united intramuscularly is made strong and the pull of the one fiber is carried on directly to the neighboring fiber. Fibers joined to one another longitudinally are thus able to act like a single long fiber.

In a quite similar fashion the traction of the muscle can be transmitted to the tendon, for here also there exists an immediate connection between the connective tissue portion of the sarcolemma and the fibers of the tendon. Moreover the perimysium internum between the individual muscle fibers (see below and also p. 158) passes directly into the fibers of the tendon, so that probably when the muscle fiber thickens in contraction and exerts a strong pressure upon the perimysium a transmission of the tension from the muscle to
Pl. 13, Figs. 8, 9 the tendon must follow. But this manner of union between muscle and tendon is not the only one, for many muscle fibers which are very rich in sarcoplasm, *e. g.* those of the dorsal fin of the sea-horse (Hippocampus) and certain fibers of the human tongue, show myofibrils which, having lost their striation close to the tendon-end of the muscle fiber, and having also diminished in thickness, penetrate the sarcolemmal tube and continue directly as fibrils of the tendon. There thus exists at the tendon-end of a striated muscle fiber direct continuity between myofibrils and the fibrils of the tendon bundles.

This intimate connection between the tissue of the tendon (collagenous or reticular connective tissue) and muscular tissue at the tendon end of the fiber corresponds to the intimate connection between the two tissues throughout the whole length of the muscle fiber. Thus the sarcolemma, a true structural constituent of the muscle fiber itself, is, at least in the greater part of its thickness, a connective-tissue basal membrane which blends most intimately with the very substance of the muscle fiber. In addition each individual striated muscle fiber is embedded in true collagenous connective tissue, the perimysium internum (p.158), be this ever so scanty. Again, the reticular connective tissue of the sarcolemma stands in the closest connection with this perimysium so that the union of the two varieties of tissue is the most intimate that can be conceived.

When the muscle CONTRACTS not only do the long and transverse axes of the muscle as a whole become altered but also those of the individual muscle fibers. If the transverse diameter increases in the region of the contraction it results in the transverse striation becoming lower or shorter. The appearances seen in the muscle fiber during contraction have not yet been explained in all points, the more so since it is doubtful whether the phenomena observed in the great muscle fibers of water beetles, so widely used for such studies, can be applied without modification to the muscle fibers of man. However it appears that the two chief substances of the fibrils, the isotropic and the anisotropic, are not involved in contraction in quite the same way. On the contrary the shortening of the fibrils is brought about entirely by the anisotropic substance which becomes shortened to less than half of its length, at the same time naturally becoming correspondingly thicker; while a shortening of the isotropic substance, at least in the large muscle fibers of many aquatic beetles, does not occur.

Just as the striated muscle fiber is more highly developed in its structure than is the unicellular fiber of smooth muscle, so also is it decidedly different in its histogenesis. The chief mass of the striated musculature comes from the myotomes of the embryonic somites which give rise directly to the dorsal trunk musculature, probably also to the ventral trunk musculature, and doubtfully to the musculature of the extremities. Myosepta of connective tissue separate the individual myotomes. But it is also certain that striated muscle may be derived from the same source as is smooth muscle, that is to say from the embryonic mesenchyme, *e. g.* the muscles of the tongue, face, and larynx, and perhaps also those of the extremities.

The cells which form the embryonic myotome are called myoblasts; at first uninuclear, they grow in length while the number of their nuclei increases by division. Gradually fibrils appear in their protoplasm, very few at first, they steadily become more numerous. It is a justifiable assumption that the fibrils are formed through the activity of mitochondria (p. 4), but they can also increase in number by a process of longitudinal splitting. Thus the young striated muscle fiber, quite short at first, is gradually formed from the myoblast and extends from one myoseptum to the next.

When fibers of striated muscle arise from embryonic mesenchyme (p. 52), there occurs the differentiation of a certain number of the mesenchyme cells into young muscle fibers in which approximately the same process of development may be recognized as has already been briefly described for the myoblasts. Those cells of the embryonic mesenchyme which are not transformed into young muscle cells become, as elsewhere, the cells of connective tissue; so that by this cellular continuity within the mesenchyme the primary intimate connection still remains between the striated muscle fiber and the connective tissue. Among other matters, these mesenchymatous striated muscle fibers show that the continuity of the myofibrils with the connective-tissue fibrils of the tendon is absolutely primary.

A sarcolemma is lacking in embryonic muscle fibers, but is gradually formed during the course of their development.

3. Cardiac Muscle

The third variety of muscular tissue found in man and in almost all vertebrates is the Pl.12, Figs.9-11
muscle of the heart wall or myocardium. It resembles striated muscle in so far as its Pl.13, Fig.10
elements are similarly striated, but differs considerably in other regards. In many of the lower vertebrates (amphibia) the form of the fibrous elements composing cardiac

muscle is more nearly related to that of smooth than to that of striated muscle. Moreover in man the relations as regards innervation are entirely different from those of striated muscle and are almost the same as those found in smooth muscle. In addition the nuclei of both smooth and cardiac muscle show the same relations.

The structural elements of cardiac muscle, however, are composed of essentially the same constituents as are those of striated muscle, viz. sarcoplasm, striated fibrils, nuclei, and sarcolemma. For the striation is produced (probably, see p.104) by striated fibrils just as in the ordinary striated fibers of the skeletal muscles. At the same time the cardiac muscle fibers, which may well be called the structural elements of cardiac muscle, differ decidedly from those of striated muscle in diameter and in form. In the first place they are rarely even approximately cylindrical but are irregular prisms with rounded edges and inconstant form; so that they do not give even approximately round cross sections, their surfaces being often grooved etc. They send out at acute angles branches which anastomose with neighboring fibers. These branches are of smaller diameter than is the main fiber but even the main fibers are decidedly thinner than those of the striated fibers of skeletal muscle, being only 10—25 μ thick. Most important of all, they are very short. Because of simplicity in description it will be assumed at once that the transverse lines which are termed intercalated discs are cell boundaries; a thing which in the full sense of the word they certainly are not. On this basis the length of the fiber of cardiac muscle is only about 50—120 μ and every such fiber has only one nucleus, rarely two, lying CENTRALLY in the fiber.

In addition the cardiac muscle fibers (to use this old name for the sake of simplicity in description) are uncommonly rich in sarcoplasm, which is much more abundant in them than it is in any of the fibers of the skeletal muscle. As a mass of sarcoplasm free from fibrils, it surrounds the nucleus which is placed quite centrally in the fiber. This nucleus is large, somewhat ellipsoidal and often shows quite irregular, even angular, contours. It may be double but in the majority of cases only a single nucleus lies in each segment, for so must be termed the region situated between two intercalated discs. Although without exception this nucleus is larger than even the largest nuclei of the fibers of skeletal muscle, it never even approximately attains their length inclining rather towards a spherical form. But the most important difference from the fiber of ordinary striated muscle is that the nucleus does not lie beneath the sarcolemma but occupies a central position in the fiber. It usually has a distinct nuclear network with pseudonucleoli and is always separated from the fibrils by considerable sarcoplasm. Pl.12, Fig.9

The sarcoplasm of the cardiac muscle fiber is not only present in great abundance but also contains great numbers of interstitial granules which are particularly abundant in the sarcoplasm about the nucleus. These two phenomena determine the fact that the transverse striation is often very indistinct while the longitudinal striation is uniformly apparent (p.104). Cardiac muscle is thus "dark" to a pronounced degree. The granules consist of lipoids, and being easily dissolved by solvents of fats are usually no longer to be recognized in fixed preparations. Accumulations of such granules are found at the poles of the nucleus, and in the cardiac muscle of old age they have an especially dark brownish color because they contain lipofuscin.

The central, perinuclear mass of sarcoplasm is always much longer than the greatest length of the nucleus; so that the center of the short cardiac muscle fiber is occupied in the greater part of its length by a core of sarcoplasm which tapers towards the ends of the fiber. From this central axis of sarcoplasm there proceed to the surface of the fiber septum-like prolongations which are almost radial in arrangement and are particularly distinct in fibers of the greatest diameter. These prolongations separate muscle columns which are often quite irregular in form, although they are usually three-sided prisms and consequently are triangular in cross-section. Thus the muscle columns as a rule have an entirely different form from those of the skeletal muscles. A transverse section of a fiber of cardiac muscle is easily distinguished from that of an ordinary striated fiber by this manner of arrangement of its muscle columns. The triangular areas of Cohnheim in the cross section of the fiber of cardiac muscle are often further subdivided by delicate septa of sarcoplasm. If the fiber is sectioned beyond the region of the nucleus there is seen the central thread of sarcoplasm, which in fixed preparations usually appears like an almost empty space because the interstitial granules have been dissolved.

Finally the fiber of cardiac muscle possesses an external sheath, a sarcolemma which is so much thinner and more delicate than that of the fibers of skeletal muscle that its presence has been questioned by many. However there is no doubt of its existence. Its composition is essentially the same as that of the sarcolemma of ordinary fibers of striated muscle, that is to say it is a membrane formed of reticulum fibers (p. 105).

As already briefly mentioned, fibers of cardiac muscle show lateral branches which leave the main part of the fiber containing the nucleus at an acute angle, and connect it with its neighboring fibers. These branches are always of much smaller diameter than is the main part of the fiber and, as mentioned, they contain no nuclei. The number of such branches is small. A single fiber usually has but one, or rarely two, such lateral processes, which may be either long and thin or short and thick. They bring about anastomosis between neighboring fibers and this produces in turn a netlike arrangement throughout the whole mass of cardiac muscle, the meshes being close and narrow, but long.

Pl.12, Fig.10
Pl.13, Fig.10

The individual fibers of cardiac muscle, as it is usually expressed, but more properly the individual segments of cardiac muscle, are separated from one another by peculiar transverse lines which often have a step-like form. On examination of cardiac muscle in the fresh condition they appear strikingly bright, for which reason the non-committal name of "BRIGHT LINES" has recently come into use. The nature of these structures has not as yet been explained. The view that they are cell boundaries, which at first is very plausible, cannot be correct because the fibrils pass through these bright lines without interruption. However, the point of view may still be supported that they are the bounaries of cell territories, *i. e.* districts of protoplasm within a network of cells, each containing one nucleus and thus corresponding in value to a cell with complete boundaries. For in the district between two intercalated discs there is, with great uniformity, just ONE nucleus.

Pl.12, Figs.10, 11
Pl.13, Fig.10

It must also be borne in mind that cardiac muscle is derived from the mesenchyme of the visceral lateral plate, consequently from an embryonic cell-net which, in a certain sense (p. 31) is still somewhat different from a true syncytium. If such a cell-net — and particularly the individual cells of the net — becomes transformed into elements of cardiac muscle, the resulting musculature will still retain with little alteration the character of a true synctium; and will itself become a cell-net. That is to say, all the cells of cardiac muscle retain a net-like connection, as indeed is actually the case; but the boundaries of the individual cell territories would still be recognizable without preventing the fibrillar contractile material penetrating these cell boundaries. However, the intercalated discs are lacking in embryonic cardiac muscle. Recently this fact has been brought into relation with the very different possibilities of nourishment in the thin embryonic and the thick adult fibers of cardiac muscle; the intercalated discs being held to render possible the nutrition of the adult fibers. But if the intercalated discs cannot be considered as true cell boundaries (such as are found in epithelial tissue) they can still be called structures which have the value of cell boundaries.[1]

Pl. 12, Fig. 11 It is a peculiarity of these intercalated discs that they rarely run in a straight line across the axis of the fiber, usually they show distinct step-like interruptions. The disc thus consists of several segments placed at short intervals from one another. This applies not merely to the discs in the main parts of the fibers but also to those in the anastomoses.

The transverse striation of cardiac muscle corresponds almost exactly to that of the fiber of ordinary striated muscle, only as a rule the striae are more delicate; otherwise the striation is the same. In particular the Z-line of cardiac muscle is usually distinct and its connection with the sarcolemma recognizable.

Since the intercalated discs cannot be regarded as true cell boundaries the entire cardiac musculature of man and vertebrate animals must be looked upon as an uninterrupted, syncytial cell-net. The cellular (fibrous) elements of the net show free ends only in the terminal regions of the heart, that is to say in the annuli fibrosi of the aortic and pulmonary roots and the terminations of the veins in the atria; in the latter situations the fibers of cardiac muscle gradually lose themselves in the walls of the veins.

The fibers of cardiac muscle are surrounded by connective tissue, but the latter is frequently present in only very small quantity, so that the individual muscle fibers, as a rule, are separated only by reticulum fibers; however the reticular frequently passes over into collagenous connective tissue. The numerous capillaries of the cardiac musculature, and slender non-medullated nerve fibers and their branches, run in this connective tissue.

The muscle fibers or cells of the atria are less complicated in structure than those of the ventricle and in particular show quite simple, steplike terminations. In many vertebrates there occur imperfectly developed muscle fibers the so-called fibers of Purkinje. These are long cells with partial differentiation of the protoplasm into contractile, transversely striated fibrils. The latter clearly pass through the cell boundaries and thus connect the neighboring cells to which they belong in common. They recall the cardiac muscle fibers of lower vertebrates (frog) which resemble smooth muscle cells but contain striated elements. In man, the structures corresponding to Purkinje fibers differ but little from the remaining cardiac muscle. They are specially thick fibers, rich in sarcoplasm and poor in fibrils, and belong to the system which conducts throughout the heart the stimulus for each beat (Tawara). As a compact bundle they run within the muscular wall of the ventricle and atrium and gradually pass over into the smooth muscle of the walls of the veins. The fibers of this bundle, being so rich in sarcoplasm and irregular in form, may be recognized most clearly in the papillary muscles into which the bundle radiates.

Nervous Tissue

Notwithstanding its remarkable diversity of structure all the nervous tissue of the body is of ectodermal origin. It is formed from the embryonic neural (medullary) tube which, as the neural (medullary) plate, represents one of the earliest organs differentiated in the embryonic body. The neural plate which becomes transformed into the neural tube consists originally of embryonic epithelial cells all of which are absolutely alike. Later there occurs a differentiation; certain of the cells are transformed into NEUROBLASTS, that is to say, into the ancestral cells of the true nervous elements of nervous tissue. The other cells become SPONGIOBLASTS, the mother cells of the NEUROGLIA, that is of the supporting substance of nervous tissue. However a part of the cells of the embryonic neural tube do not suffer further differentiation but remain in an embryonic, epithelial condition. Such are the cells of the laminae chorioideae epitheliales of the venous plexuses and the telae chorioideae; while the so-called ependymal epithelium represents a transition from the epithelial stage of development to that of glia cells.

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[1] Thus the fibrils pass through the boundaries of the so-called fibers of Purkinje which without doubt are to be considered as cell boundaries, even if they are only present in the outer zone of the protoplasm. These fibers are beyond question cells which are delimited one from another.

Accordingly nervous tissue in the adult consists of two chief constituents, the neuroglia, and the nervous elements proper, *i. e.* the neuroblasts which have become transformed into nerve cells and have developed processes. Since the nerve cells frequently send their processes to relatively distant regions of the body (as much as a meter away); and since these processes as a rule obtain special sheaths, they are referred to as NERVE FIBERS. Hence the conception, long current, that nervous tissue essentially consists of 1. nerve cells, 2. nerve fibers, 3. neuroglia.

According to the views prevailing at present a nerve cell and its fiber (at least the chief constituent of the latter, the axis cylinder, and perhaps even the whole fiber) including also the terminal expansion of the fiber in the periphery of the body, all form a unit, the so-called **neurone** (neurodendron). The conception of the neurone finds support in the mode of development of nervous tissue. The neuroblasts of the embryonic neural tube send out from one pole of their body, which is usually conical, a process towards the periphery where later the terminal expansion is formed. This process becomes the axone (or neurite) of the nerve cell, and forms the so-called axis cylinder of the future nerve fiber; retaining all the while its connection with the neuroblast as the latter develops and becomes the nerve cell. Probably the outgrowth of the nerve fiber takes place along a specially preformed pathway.

Thus, according to the neurone theory, a nervous unit or neurone consists of 1. the NERVE CELL, the true centre of the neurone in the trophic sense, 2. the NERVE FIBER formed of the axone with its sheaths, 3. the terminal expansion at the surface of the body, the so-called telodendron. According to the claims of the neurone theory, all neurones must be independent and cannot be directly connected with one another. The transference of a stimulus from one neurone to another can only take place through contact, *e. g.* through collaterals of the axone which branch around the centre of another neurone, *i. e.* around another nerve cell. Thus according to the theory the telodendria of each individual neurone must remain independent, a view which is scarcely tenable since the occurrence of distinct networks of telodendria has long since been established beyond question.

In the present state of our knowledge, it may be taken as certain that the hypothesis of the formation of the nervous system out of completely separated units, the neurones, must fail. Not merely in the region of the telodendria has continuity been demonstrated between separate neurones, but uninterrupted connection between the branches of the dendrites of nerve cells has also unquestionably been observed. In spite of this, the neurone theory is a convenient basis, so to speak, for the following description even though in the course of time it should indeed be proved untenable.

1. Nerve Cells (Ganglion Cells)

The nerve cells of the central nervous system occur chiefly in its grey matter; they are found also in certain sense organs such as the retina of the eye and the olfactory mucous membrane, also in the plexuses and ganglia of the cerebrospinal and sympathetic nervous Pls. 14, 15 Pl. 16, Figs. 1–7 systems. The form of nerve cells is highly variable; they are often polyhedral and frequently spherical; usually they are strongly branched but in many cases are altogether devoid of such processes. On the other hand they frequently show very highly individual forms, as in many portions of the central nervous system, particularly in the cerebellum. A few characteristic and peculiarly bizarre forms are exclusively confined to very definite localities of the nervous system.

Nerve cells (a term to be preferred to the much used, synonomous expression, ganglion cells) are, in general, large cells with abundant protoplasm but without cell membranes. They are among the largest cells of the body, only a few of their many varieties being small cells with scanty protoplasm. The size varies from 5 μ to almost 150 μ.[1]

Nerve cells have long been known as unipolar, bipolar, or multipolar, according to the number of their processes. In this connection, two kinds of processes must be considered, the nerve process, axis-cylinder, neurite or **axone** and the **dendrites** which are protoplasmic processes essentially of the same character as the protoplasm of the cell. The dendrites uniformly outnumber the axones. The AXONE takes origin directly from the cell body as a small cone (cone of origin) and usually, but not invariably, transmits impulses from the cell outward, cellulifugal impulses. It is a delicate process usually very long and of about equal thickness throughout all its course as the axis cylinder of a nerve fiber. As a rule it is but little branched although a few delicate, lateral branches, so called collaterals, may arise from an axone. On the other hand, the DENDRITES usually transmit cellulipetal impulses and are very thick, arising from the cell by a broad origin which shows no demarcation between cell and dendrite. They branch in treelike fashion and according to the neurone theory have no direct connection with other nervous elements. Usually the cell body simply tapers off in several directions into as many stout dendrites; only in rare cases do they spring abruptly from the cell as in the small granular cells of the cerebellar cortex. The dendrites of many nerve cells branch to quite an extraordinary degree and often spread over an exceedingly wide area, many times as great as that of the cell body. Only the so-called multipolar nerve cells possess dendrites in addition to an axone. Unipolar and bipolar nerve cells have axones only. The terms unipolar, bipolar and multipolar, which unfortunately have long been fixed in usage, are not altogether precise and free from objection, seeing that they relate at times to the axones, and at other times to the dendrites.

The PRINCIPLE TYPES of nerve cells may be grouped into the following subdivisions according to the main features of their form and processes. (For a more detailed description see page 116 also the chapter on the central nervous system, page 160).

1. SMALL SPINDLE- OR PEAR-SHAPED epithelial-like nerve cells, WITHOUT DENDRITES, BUT WITH ONE AXONE, so called UNIPOLAR cells. These occur chiefly as olfactory cells in the olfactory mucous membrane.

2. SPHERICAL nerve cells, WITHOUT DENDRITES BUT WITH ONE AXONE (UNIPOLAR cells) which soon after leaving the cell makes a T-shaped division so that the cells are, in effect, bipolar cells. This form occurs chiefly in the peripheral ganglia (spinal ganglia) of the central nervous system.

3. Cells of SPHERICAL or pear-like form WITHOUT DENDRITES BUT WITH TWO AXONES arising from opposite ends of the cells, so-called BIPOLAR cells. These occur chiefly in the

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[1] In many fishes there occur nerve cells of yet far greater size. Even in man, the size is often remarkable when the whole territory is considered over which the branches of the dendrites extend.

retina (inner granular layer) and in the ganglion of the acoustic nerve (spiral ganglion of the cochlea).

4. Large, POLYHEDRAL so-called MULTIPOLAR nerve cells of irregular shape and highly varied form, WITH ONE AXONE AND SEVERAL highly developed and much branched DENDRITES which project from the cell in all directions. To this type belong the multipolar cells of the spinal cord and medulla oblongata and of the central and internal masses of cerebral grey matter. It is a remarkably widespread type of nerve cell.

5. MULTIPOLAR NERVE CELLS OF REGULAR FORM possessing one axone and also DENDRITES WHICH ARISE from the cell body IN A DEFINITE MANNER characteristic for the type of cell, and which are often very highly branched. The chief representatives of this group are the PYRAMIDAL CELLS of the cerebral cortex and the PURKINJE CELLS of the cerebellar cortex. In the latter case, the cell develops an extraordinary superficial area through the treelike branching of its two main dendrites.

6. SMALL MULTIPOLAR NERVE CELLS with dendrites of many DIFFERENT FORMS, such as certain cells of the granular and molecular layers of the cerebellar cortex and a few varieties of cells from the cerebrum etc. Occasionally in these cases there are found two axones (?).

These six varieties of nerve cells have this in common, that their axone produces its terminal arborization only at a considerably distance from the cell, and as a rule after it has run a long course as a nerve fiber. Such cells are known as DEITER's cells (Golgi's type I) in contrast to the GOLGI cells (Golgi's type II) the axone of which after a short course usually breaks up into a very extensive arborization without having previously given off lateral branches (collaterals) as do the axones which belong to the cells of Deiter's type. This variety of cell is found only in the brain and spinal cord. In this category probably belong also a few other forms of nerve cells, *e. g.* many cells of the cerebellar cortex and a few others concerning which information is not as yet quite certain.

In all these six markedly different varieties of nerve cells found in the cerebrospinal nervous system, there may be distinguished two chief types of cells, or better of neurones (adopting this hypothesis as a basis for the presentation of the subject). First is that variety of **neurone in which the cell is terminal.** This is the case in all multipolar cells which have several dendrites and a single centrifugal axone. The second variety of **neurone has the cell situated midway** along its course. This is the case in all unipolar and bipolar cells, the cells which apparently are unipolar having developed from forms which originally were bipolar. Such cells have no dendrites but possess two axones, one cellulifugal, the other cellulipetal, proceeding from the cell body in opposite directions. These are neurones of the peripheral sensory conduction path, the cellulipetal axones of which carry sensory stimuli to the cells of their neurone; while the cellulifugal axones transmit the impulse from the cell to a more central neurone.[1] Both axones are true nerve fibers, often of considerably length, and possess the typical sheaths.

Figs. 14, 15

Pl. 15, Figs. 5, 6

Pl. 16, Fig. 5

In contrast to these cells of the cerebrospinal nervous system there stand the cellular elements of the sympathetic nervous system, representing nerve cells of a type which has remained at a more primitive stage of development. These are rather small nerve cells with approximately spherical cell bodies which give off processes. The latter in general arise directly from the cell body, and without doubt are to be considered partly

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[1] It frequently is convenient to think of the cellulipetal fibers as dendrites, the cellulifugal fibers being the true axones. — Trans. Note.

Fig. 14. **Diagram of a Neurone in Which the Nerve Cell Is Terminal: Motor Neurone.**

The upper part of the figure shows a multipolar nerve cell with its dendrites. The cell sends downward a single axone which receives a medullary sheath and thus becomes a medullated nerve fiber. After a long course, marked by nodes of Ranvier, it divides and finally ends in telodendria. The arrow indicates that impulses are conducted towards the periphery, *i. e.* are centrifugal.

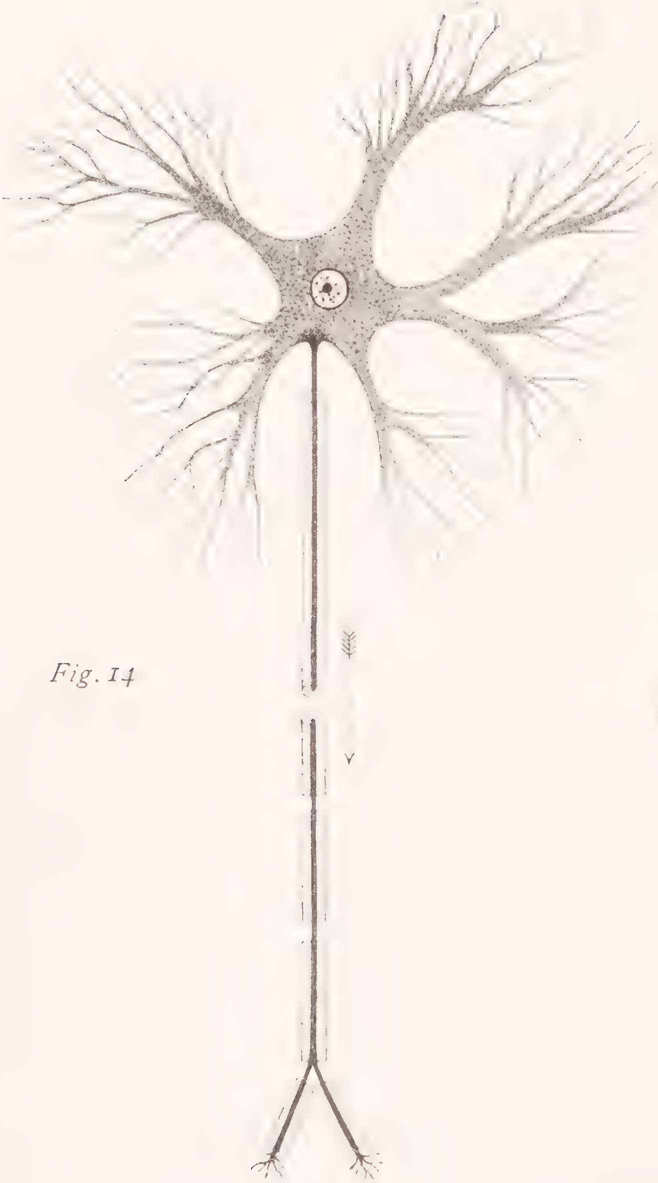

Fig. 14

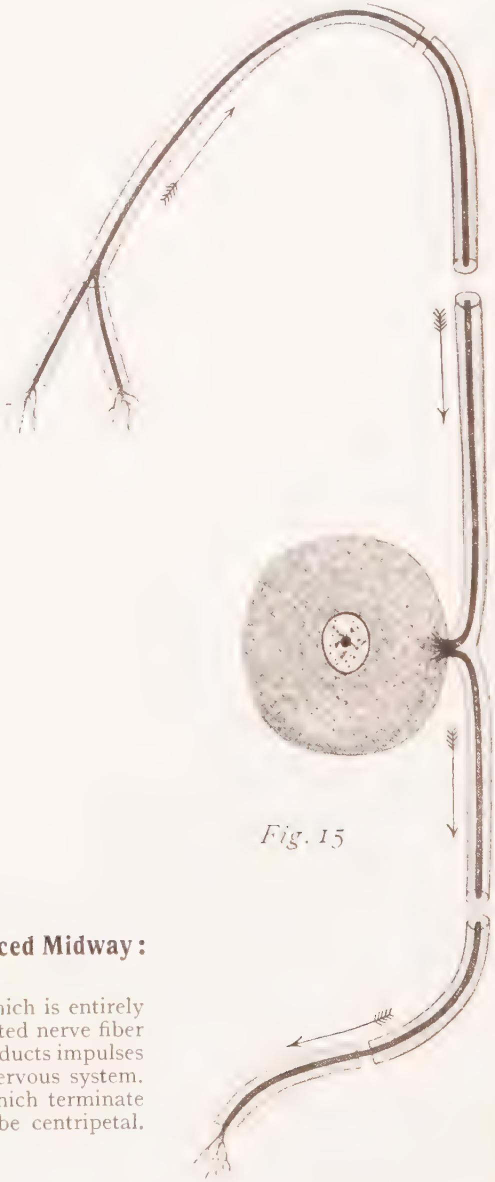

Fig. 15

Fig. 15. **Diagram of a Neurone with Nerve Cell Placed Midway: Sensory Neurone.**

Two axones arise together from a spherical nerve cell which is entirely devoid of dendrites. The upper axone consists of a medullated nerve fiber which divides at the periphery and shows telodendria. It conducts impulses towards the cell. The lower axone runs to the central nervous system. It always is a medullated nerve fiber, the telodendria of which terminate centrally. The arrows show the direction of conduction to be centripetal.

as axones and perhaps partly as dendrites (?). In any case several processes often emerge from a single cell and become true nerve fibers, usually without medullary sheaths unless their course is quite long, when they acquire a thin medullary sheath. Nevertheless, these cells, in a certain sense, are terminal as regards their neurones, and on the whole (?) their axones are cellulifugal. These cells are usually termed multipolar although among them there are a few which send out one process only (see below). In addition to occurring in the sympathetic nervous system a few such cells are also found in the spinal ganglia (p. 176).

General Structure of Nerve Cells

Nerve cells show the three chief constituents of animal cells. CENTROSOMES are demonstrable in several varieties of nerve cells although it is in the highest degree exceptional for either the centrosomes or the nerve cells to divide. The **nuclei** of almost all nerve cells show similar characteristics. They are of medium size, are almost exactly spherical, and have an extremely delicate network of chromatin and a large nucleolus. The nucleolus is very noticeable and usually catches the eye because the chromatin content of the nucleus is otherwise not at all marked. It is quite characteristic that the size of the nuclei of nerve cells varies within rather narrow limits, and is by no means proportionate to the size of the cell; so that nuclei of small nerve cells are strikingly large, and those of large nerve cells are just as strikingly small.

Pl. 14, Figs. 3, 4
Pl. 15, Figs. 1–3
Pl. 16, Figs. 6, 7

The chromatin of nerve cells frequently shows astonishingly little inclination to be colored by basic dyes but often is stained by acid dyes (so-called oxychromatin). The large nucleoli of nerve cells are often pronouncedly oxyphilic.

The CELL BODIES of nerve cells show a series of peculiarities. The protoplasm of nerve cells (also well named neuroplasm) often takes very singular forms, quite apart from those determined by the number, size and form of the dendrites. For this type of cell shows characteristic structures which extend into at least its larger dendrites. Here belongs in the first place, a peculiar type of BASOPHILIC GRANULATION known as the NISSL BODIES, or **tigroid** granules. The latter name is derived from the fact that the nerve cell appears spotted when stained with methylene blue or fuchsin. These granules are probably found in all nerve cells though in many cases their numbers are much restricted, and in a few nerve cells such as the granular cells of the cerebellum, they appear to be completely lacking. They are most strongly developed in the multipolar cells of the spinal cord and brain in which they usually appear as angular polyhedral structures of considerable, but variable, size. Often they are so abundant as to lie pressed close together within the cell body itself, and in the larger dendrites; while on the other hand they do not enter into the axone. They are easily stained with basic aniline dyes such as methylene blue, thionin, basic fuchsin etc. and appear to be albuminous bodies standing in relation to the metabolism of the nerve cell.

Pl. 16, Figs. 6, 7
Pl. 32, Fig. 4

The name CYTOCHROMATIN has been proposed for these protoplasmic inclusions of the nerve cell on the assumption that their substance is identical with the chromatin of the nucleus, or at least is closely related to it. It must be borne in mind that they occur in particularly large number and size in such nerve cells as have abundant protoplasm and only a small nucleus.

They do not always appear in the form of coarse granules; occasionally they are very fine. Thus, in the spherical nerve cells of the spinal ganglia which have no dendrites, they usually lie close together in a narrow superficial zone while the remaining part of the cell is filled with the finest of scattered granules. The cells of the sympathetic nervous system also frequently have only fine superficial granules which do not enter into their processes, the so-called dendrites. Moreover the coarser tigroid bodies are composed of a number of finer granules held together in a common matrix which in turn is connected with the general protoplasm of the cell.

The **neurofibrils** form a further constant and very important constituent of nerve cells. They are fine, usually indeed extremely fine, fibrils which singly, or more often in slender bundles, traverse the cell body itself as well as the dendrites and also enter into the axone (p. 124). Fibrillar networks, the existence of which formerly was frequently denied, are no longer doubtful according to later observations. True anastomoses between bundles of fib- Pl. 14, Figs. 3, 4 rils occur as well as fibrils in parallel and interlacing arrangements. The neurofibrils for the most part run in the intervals between the Nissl bodies. In parallel arrangement they are continued into the axis cylinder of the nerve fiber. Although the greater part of the neurofibrils within the body of the cell occupy the intervals between the tigroid granules, some of the latter, particularly the larger, are penetrated by the fibrils. Delicate threads of protoplasm connect the tigroid granules and the fibrils. Moreover it appears as though the fibrils were not homogeneous but were in turn composed of rows of extremely fine granules placed very close together.

Occasionally there occur other inclusions within the cell body of nerve cells. The most common are PIGMENT GRANULES which may be yellow, brown, or even dark brown. These are always smaller than the basophilic Nissl bodies but often occupy an equally considerable space within the body of the cell. They commonly lie close together in the neighborhood of the nucleus which is often partly surrounded by them, as by a crescent; or they may Pl. 16, Figs. 4, 7 be situated eccentrically in the protoplasm and form there a circumscribed mass. Occasionally, as in the substantia nigra and in the locus coeruleus, they impart to the entire region of the central nervous system in which they occur a color which is macroscopically visible.

Two different kinds of pigment may be distinguished in the cytoplasm of nerve cells; first, true melanin pigment (p. 15) such as occurs in the cells of the substantia nigra; and second, lipofuscin which may form in greater or less quantity in any nerve cell and frequently represents a phenomenon of aging (p. 16). This lipoid pigment is pale and varies from yellow to yellowish brown. Pigment is never found in the dendrites of nerve cells but is always confined to the central region of the cell body.

Structures which are not confined to nerve cells alone, although they nowhere stand out so suggestively Pl. 2, Fig. 8 as in the latter, are 1. the RETICULAR APPARATUS OF GOLGI, a network of threadlike cords which may be demonstrated by the aid of certain reagents but the significance of which is as yet uncertain (also known as the internal reticular apparatus of nerve cells, p. 6). 2. delicate canal-like structures within the cell body which probably are connected with the pericellular lymph spaces and together are known as the TROPHOSPONGIUM.

Special Features of the Various Types of Nerve Cells

As regards the features of the individual varieties of nerve cells of the DEITERS' type, many special forms which are restricted in their occurrence to certain regions will be described in the presentation of the organ concerned. However it is well to describe at once the chief forms of nerve cells.

Pl. 14, Fig. 1 One type of nerve cell commonly occurring in the central nervous system is the so- Pl. 16, Figs. 1, 6 called **multipolar** NERVE CELL which appears as the sole form of nerve cell in the grey Pl. 32, Fig. 4 matter of the spinal cord and is also found generally within the brain, with the exception of the cerebral and cerebellar cortices. This is a type of cell the size of which is highly variable. Some are very large cells such as the root cells in the anterior horn of the spinal cord and in the motor nuclei of the cerebral nerves; while others are remarkably small, as for instance the cells of the substantia gelatinosa posterior and many of the masses of the grey matter of the brain. The cell body of the largest of such cells attains a size of about

100 μ while the smallest forms scarcely reach a tenth of this size. The nuclei reach a diameter of almost 20 μ and even in the most bizarre forms always are strictly spherical. The main portion of the body of the cell from which the processes emerge has usually an irregularly polyhedral form and thus appears polygonal in cross section, usually showing five or six sides. Although a few cells appear quadrilateral or triangular these are commonly the smaller forms, some of which may even present a fusiform figure, so that the elongated cell body appears like a thickening between two dendrites which spring directly from its ends. Tigroid granules occupy the entire extent of the cell body including the dendrites, within which they are more or less attenuated according to the thickness of the dendrite. In the larger cells of this class the tigroid granules reach their maximum size and show a rather uniform distribution. Numerous neurofibrils may also be demonstrated and frequently pigment as well.

This type of cell has always a single cellulifugal axone upon which it is terminal and also several dendrites which emerge so gradually from the body of the cell as to constitute direct elongations of the latter. The protoplasm of the cell body passes so gradually into the dendrites that it is impossible to determine a boundary between cell body and dendrite. That is to say, the trunk of the dendrite, bearing as yet but few branches, shows exactly the same structure as does the protoplasm of the cell body proper and contains quite large tigroid bodies and neurofibrils (p. 116). On the other hand it never contains pigment. The dendrites branch in a treelike fashion and this arborization often extends over quite a large area which may be several times as great as the main part of the cell. The finer the branches of the dendrites become the smaller and less abundant do the tigroid bodies appear; and a like reduction occurs in the number of the fibrils which now show a more or less parallel course. The very finest of the branches of the dendrites appear to be purely protoplasmic extensions of the cell, however they no longer contain tigroid bodies. They pass into a neuropil (p. 121).

Most of these so-called multipolar cells send out dendrites from all sides or corners of the cell body. However there are cells belonging to this class in which the dendrites pass out from the body of the cell in only one direction, while the remaining part of the surface of the cell is rounded and sends out no dendrites. This is notably the case with the Purkinje cells of the cerebellar cortex and with the cells of the ganglion nervi optici of the retina. In both cases, but more especially in the first, the dendrites are branched to an extraordinary degree.

The "multipolar" nerve cell has more than one axone which however is decidedly different from the dendrites. In the first place it proceeds directly from the cell body, usually only a small conical projection marking the spot. This axone, the diameter of which in general depends upon the size of the cell (p. 124) is unbranched (as to collaterals, see p. 113) and is completely devoid of tigroid bodies. On the other hand neurofibrils enter it and there run parallel courses. These fibrils are derived partly from the cell body itself and partly from the related dendrites. While the axone becomes the axis cylinder of a medullated nerve fiber the dendrites become branched and contribute to the formation of a neuropil. Pl. 16, Fig. 1

Closely related to this widespread type of multipolar nerve cell stand certain cells of the cerebral and cerebellar cortices which also are terminal in their neurones and which are to be distinguished only through peculiarities in the behavior of their dendrites. Here belong in the first place, the pyramidal cells of the cerebral cortex and those related cells of the bulbus olfactorius which are known as the mitral cells; also the PURKINJE cells of Pl. 14, Figs. 2-4 Pl. 14, Figs. 5, 6 the cortex of the cerebellum which will be more fully described under that organ. The so-called polymorphous cells of the deeper layers of the cerebral cortex represent all forms of transition between the pyramidal cells on the one hand and ordinary multipolar cells on the other.

Other forms of cells in the central nervous system differ somewhat from the above, *e. g.* the small granular cells of the cerebellar cortex, which have slender dendrites proceeding directly from the cell body and whose protoplasm contains no tigroid bodies. Other cells of the cerebellar cortex also occupy a certain exceptional position (see p. 113 and the description of the cerebellum).

As mentioned, the so-called multipolar cells are found only within the central nervous system. Like all the nervous tissue elements of the organs of this system, they are embedded in neuroglia (p. 128). In particular, certain varieties of glia cells lie close to the bodies of the larger nerve cells and on this account bear the name of satellite cells.

A type of nerve cell which departs from the multipolar form is seen in that group in which THE CELL DOES NOT OCCUPY A TERMINAL POSITION BUT IS SITUATED ALONG THE COURSE OF THE NEURONE (p. 113). These are cells of the peripheral ganglia, spinal ganglia, and ganglia of the acoustic and other cranial sensory nerves. To this category belong the so-called unipolar and bipolar cells. The outstanding characteristic of this type of nerve cell is that it has no dendrites but, corresponding to its position in its neurone, sends out two axones (see p. 113 and *Fig. 15*). The fact that the cell lies midway in its neurone is more apparent in bipolar than in unipolar cells. But the latter are derived from bipolar forms, and in their embryonic condition were bipolar cells.

The so-called **unipolar cells,** such as occur in the spinal ganglia and the ganglia of the nervus trigeminus, nervus intermedius, nervus glossopharyngeus and nervus vagus are large cells, almost exactly spherical and quite without dendrites. Apparently they send out
Pl. 15, Figs. 1—3 but a single axone (p. 113). After a very short course this axone usually divides in a T-like
Pl. 16, Figs. 2—4 or Y-like manner. The diameter of the body of the cell may reach almost 100 μ; however there occur scattered cells of this type of only medium size (60 μ), and others still smaller (p. 176). The cell body surrounds a nucleus which in turn is almost a true sphere and is remarkable because of its small content of chromatin. It always contains a large nucleolus which usually is oxyphilic (p. 115).

During youth the cells of the spinal ganglia are practically spherical; small departures from this form when seen in a preparation are for the most part to be considered as artefacts. But in old age the surface of the cell becomes more or less decidedly irregular, so that even fenestration may occur. That the alleged dendrites of these cells, which are said to be present within the capsule, may arise in this manner cannot be fully substantiated.

Usually the nucleus lies somewhat eccentrically but not far from the middle of the cell. The cell body contains tigroid granules which as a rule are decidedly smaller than are those of "multipolar" cells. These granules are by no means uniformly distributed in the cell body; but either form concentric rings about the nucleus or show a marked accumulation near the surface of the cell, and a second one close to the surface of the nucleus. However, many small types of cells in the spinal ganglia have coarse granules evenly distributed throughout the whole body of the cell, as are those of multipolar cells, but these cells are probably a special type (p. 176).

The protoplasm of ganglion cells contains numerous neurofibrils which fill the whole
Pl. 15, Figs 1—3 body of the cell with a close network and extend into the axone. The latter in proportion to the size of the cell is relatively weak. It arises from the spherical cell body by means of a short cone of origin, and having divided in a T- or Y-like fashion at a greater or less distance from the body of the cell it becomes surrounded by a medullary sheath. Frequently the axones,

or the branches into which they divide, form loops around the nerve cells before they enter on the course to their destination.

Yellow pigment (lipofuscin) is very commonly found in adult spinal ganglion cells, Pl. 16, Fig. 4 usually it lies in a mass eccentrically within the cell body. Melanin pigment is never found.

Since a cell in a spinal ganglion does not lie within the central nervous system, it is not embedded in neuroglia as are the cells of the brain and spinal cord, but is surrounded by a sheath similar to that of the other elements of the peripheral nervous system. In the first place it is surrounded by the neurolemma or sheath of SCHWANN which is really the continuation of the neuroglia into the region of the peripheral nervous system (p. 126). The neurolemma in this situation (and in nerve fibers also) is probably syncytial in nature and consists of an extremely delicate protoplasmic sheath which contains nuclei and lies upon the surface of the nerve cell. The nuclei of the sheath are relatively large and numerous. They may even produce slight dimples in the surface of the nerve cell. No demarcation of the protoplasm into areas belonging to the individual nuclei can be seen with certainty; although the terms "mantle cells" and "amphicytes" are used. The cells are said to have a branched outline, in which case they would form a cell net. External to this neurolemmal sheath there lies around the cells of the spinal ganglion a second sheath which is of connective tissue and which corresponds to, and is continuous with, the endoneural sheath of the nerve fiber arising from the cell. In it there may be recognized flat connective tissue cells and their nuclei.

The **bipolar cells** of the ganglion of the acoustic nerve show quite similar features. Pl. 15, Fig. 4 These cells are smaller than the unipolar cells of the spinal ganglia; on the whole their bodies are spherical but somewhat drawn out where the two axones leave at the opposite poles. The nuclei of these cells are proportionately larger than those of the spinal ganglia but otherwise agree with them in their essential structure. The axones are rather stout and almost immediately after they leave the cell body become surrounded by a medullary sheath. They never twine about the body of the cell. The sheaths of these cells are similar to those of the cells of the spinal ganglia.

Another special type of nerve cell which differs fundamentally from the foregoing is the so-called NEURO-EPITHELIAL CELL, *i.e.* a nerve cell which looks like an epithelial cell but from which there proceeds a true axone. Such cells are rare in man and other vertebrates, Pl. 81, Fig. 1 but are found as olfactory cells in the epithelium of the mucous membrane of the regio olfactoria; Pl. 87, Fig. 2 and also occur in a modified form in the retina of the eye.

The CELLS of the **sympathetic** NERVOUS SYSTEM form a category which differs markedly from the types previously described. Although not all the cells of this system conform fully to the type about to be described, yet the variations are relatively small, and very unimportant. Sympathetic nerve cells may be described by the useful, but objectionable (p. 112), Pl. 15, Figs. 5, 6 term "multipolar", because as a rule they send out several processes from different points Pl. 16, Fig. 5 of their body. Almost all these processes show the same structure; so that a distinction between dendrites and axones, such as is present in the much more highly differentiated cells of the cerebrospinal system, does not as a rule seem to be possible for the cells of the sympathetic system. However, to a certain extent, these cells must be regarded as terminal in their neurones; just as are the multipolar cells of the central nervous system.

The body of the sympathetic nerve cell usually is approximately spherical and decidedly smaller than that of the spinal ganglion cell. It measures only 20—40 μ in diameter, but occasionally is larger (up to 50 μ). Otherwise at first glance the form of the cell resembles that of a spinal ganglion cell, particularly in regard to its sheaths (see below). Consequently Pl. 16, Fig. 5

Pl. 34, Fig. 4 under ordinary methods of staining, which do not demonstrate the processes, these cells might at first be readily mistaken for the small cells of a spinal ganglion. However they are to be distinguished from the latter by frequently possessing two, and occasionally three nuclei; a thing which is never found in any type of cell of the cerebrospinal system. The processes of the cell may be either thick or thin and their number is variable. Especially in the case of large cells the number of processes may be large, even reaching twenty; while in small cells the number will be much less. All the processes show essentially the same features quite independently of their size. They arise almost directly from the body of the cell, although frequently a short conical projection marks their origin. Like the body of the cell itself the processes consist of neuroplasm and neurofibrils and usually are very long and devoid of branches. Occasionally they are distributed uniformly in the area surrounding the cell; yet it does happen that they may be confined to a narrowly restricted region of the cell body, in which case the latter commonly assumes the shape of a pear.

The body of the sympathetic nerve cell contains numerous fine neurofibrils which are much interwoven, but which become parallel to one another when they enter the processes. The tigroid substance appears partly as coarse granules, partly in a fine dustlike form, and is confined to the body of the cell. Lipoid pigment occurs particularly in old age, just as in the cells of the spinal ganglia.

The thickness of the processes is extremely variable. In their course, they penetrate the capsule and, at least in part, become the axis cylinders of fibers which usually, but not Pl. 15, Fig. 6 invariably, are non-medullated. There is no doubt that from the one sympathetic nerve cell there arise several processes which become nerve fibers, and which must consequently be described as axones. But the other processes also, which do not show a transition into nerve fibers, resemble the latter both in structure and in behavior. Consequently to characterize them simply as dendrites is not permissible; because apart from a few collaterals, such as may be present on true axones, they do not as a rule show an arborization in the same sense as do the dendrites of cells of the cerebrospinal system. Dichotomous division of the processes of sympathetic nerve cells also occurs.

In its structure, the sympathetic nervous system stands, so to speak, at a much less developed and more embryonic stage than does the cerebrospinal. This shows in the first place in the cell itself, in which processes are present with the presumable function of carrying the nervous impulse, but which cannot strictly be classified either as axones or as dendrites. Except for the so-called "end plates" free endings of the processes are never observed; so that it is necessary to assume a plasmodial structure for the sympathetic nervous system as a whole, nerve cells separated by wide intervals being connected by means of their long processes.

The one and only type of free termination which has been observed for the processes of sympathetic nerve cells is the so-called END PLATE. This plate is the thickened, clublike end of a process which has run a longer or shorter course (usually the latter) and in its terminal expansion still shows, like the cell itself, the presence of neuroplasm and neurofibrils. In addition there have been observed, around sympathetic nerve cells, basketlike networks which always consist of several fibers, and do not represent specific terminations.

When in a section the processes of a sympathetic nerve cell are cut off, the cell appears to have a rounded, somewhat stellate body. This applies particularly to the larger types of cells with abundant processes which Pl. 15, Fig. 5 at first are entirely devoid of branches. The smaller types of cells commonly possess two nuclei and often send out only one or two processes, and consequently do not deserve the name multipolar. They have very irregular cell bodies which by no means recall the approximately spherical or pear-like form of the larger cells.

Various other types of sympathetic nerve cells have been described and arranged in ill-defined groups on the basis of alleged differences of behavior on the part of what are erroneously regarded as dendrites. Thus in many quarters intra- and extra-capsular dendrites have been described. The latter are said to possess branches which however are not demonstrable by the recent and more exact methods. It is equally doubtful if there are dendrites which branch immediately around the cell body within the capsule; and the description of nerve cells with surfaces irregular to the point of fenestration, is to be received with skepticism. (On this point see the discussion on cells of the spinal ganglia.) Now, as ever, it is more than doubtful whether nerve cells of the sympathetic system give rise to centripetal fibers and are consequently to be considered as sensory cells. Should such be the case, the peripheral sensory neurone must be constructed quite differently from that of the cerebrospinal system (p. 113). On the other hand scattered sympathetic nerve cells occur in the spinal ganglion.

As regards their sheaths the sympathetic nerve cells resemble those of the spinal ganglia, which also lie outside of the central nervous system. They have a sheath of Schwann and an endoneural sheath, but neither are as well developed as around the cells of a spinal ganglion (p. 119). The nuclei of the neurolemmal sheath are often very few, so that the existence of this sheath is strongly questioned in many quarters; and the connective-tissue endoneural sheath is often merely indicated in the case of certain small cells; although it usually is quite well developed in the larger cells. As already mentioned the long processes of the nerve cells penetrate these sheaths. Only the short types of end plates terminate within sheaths.

Pl. 16, Fig. 5

Additional Cellular Formations of the Nervous System

Related to nerve cells in their origin are certain cells which preserve their embryonic epithelial character throughout life. These cells arise from the same source as do the young neuroblasts which originally have (p. 110) the same characteristics, but later develop into the true nerve cells. There are two varieties of these cells: 1. **EPITHELIAL CELLS OF THE VENOUS PLEXUSES** and of the telae chorioideae, cells of the so-called laminae chorioideae epitheliales. 2. the so-called **CHROMAFFINE CELLS OF THE PARAGANGLIA** of the sympathetic nervous system.

Pl. 30 Fig. 6

As regards the former, the epithelial cells are nearly related to those of the ependyma and consequently for convenience will be dealt with more fully in the description of the neuroglia.

The chromaffine cells will be discussed in connection with the organs concerned.

The Connections of Neurones with One Another, the NEUROPIL

According to the view which prevails at present, (the basis of which, as already indicated, has been severely shaken) each nervous unit or neurone is in itself a complete structure and is not directly continuous with any neighboring neurone. When the nervous impulse, as is usually the case, must pass through several associated neurones, and thus must be carried on from one neurone to another, there occurs a connection which though very extensive is entirely one of contact. This contact takes place between the nerve cell, *i. e.* the cell body of the one neurone, and the telodendron of the other neurone; without (at least according to the neurone theory) any constituent of the one neurone passing continuously onward into the other neurone.

Pl. 14, Fig. 6

However, even if we exclude direct passage of a conducting material from one neurone to another the contact between two neurones is a very intimate one. It occurs through a remarkably close interweaving of the most delicate branches of the dendrites of the one cell with the finest terminal branchings of the telodendron of the axone of the other cell. These extremely fine branchings enter into numerous mutual contacts through which the impulse passes on from one neurone to the other.

According to this conception of the neurone theory, there takes place on the part of the two neurones, an extensive contact by means of which the impulse passes on from one neurone to the other: but the conducting material as such is interrupted at the points of contact by the smallest possible interval.

It is frequently assumed – and the assumption is justified by the structure of the nervous elements – that the neurofibrils represent the conducting material. According to another conception, which is also based on the structure of the nervous elements, the neurofibrils have only the function of support, thus representing a variety of tonofibrils. In this case the true conducting material would be the neuroplasm itself.

As repeatedly mentioned, the neurone theory in the form set forth above (p. 111) is no longer tenable, for recent methods of investigation have shown beyond doubt that the individual neurones are not completely independent structures. The direct passage of the dendritic arborization of one cell into that of a neighboring cell can now be demonstrated with certainty. Also a similar merging of the neighboring telodendria of axones has been shown; and finally also a direct connection between the telodendria of the one neurone and the arborization of the dendrites of the other and associated neurone.

In all places in the central nervous system where neurones are linked together in the manner described, there is seen the interweaving of arborizations from telodendria and from dendrites. Frequently these interlacements occur in special districts or more or less sharply defined layers in which neither nerve fibers nor the bodies of nerve cells are to be found, but in which the delicate arborizations lie embedded within an equally delicate framework of neuroglia.

Such an area, frequently occurring in the form of a zone or layer, is conveniently known as a **neuropil**. Before there were available methods of investigation suitable for re-
Pl. 14, Fig. 6 vealing the delicate branchings of nerve cells, there was uncertainty as to the structure of such layers of the nervous system; a fact which is expressed in the older names, such as molecular layer.

Two facts show well that it is the dendritic branching which is primarily responsible for the connection by which the impulse passes between neighboring and associated neurones. First, only those cells possess dendrites which are in a good position to receive stimuli from an associated neurone; consequently on this basis the unipolar nerve cells of the spinal ganglia are without dendrites. (This statement has regard to the behavior of the cells of the cerebrospinal nervous system only; cells of the sympathetic system show quite different relations. See p. 120.) Second, the multipolar nerve cells develope dendrites on that side only from which they can receive an impulse from an associated neurone. Consequently there are multipolar cells (p. 117) which send out dendrites on all sides; and others the dendrites of which run always in a quite definite direction, namely that from which the impulse shall pass to them. Thus in many multipolar nerve cells, the dendrites emerge together from one pole of the otherwise spherical cell body.

In addition to the true neuropil, it appears that the transmission of the impulse from one neurone to another may occur through the telodendria which come from one or more axones and are woven around the cell body of another neurone. The telodendria are in contact with the body of the cell, by means of so-called terminal bulbs.

2. Nerve Fibers

Pl. 16, Figs. 8-10 For a long time, nerve fibers were held to be independent formations and their connec-
Pl. 17 tion with nerve cells was unknown. Now, it is known that a nerve fiber, notwithstanding its length which is often extreme, represents nothing but the process of a nerve cell, *i. e.* its axone (p. 111). Thus every bare axone represents the nerve fiber of a definite nerve cell; however such axones, should they have a long course, are usually surrounded by special sheaths. Thus the term, NERVE FIBER commonly INDICATES a structure formed from THE AXONE OF A NERVE CELL AND THOSE ELEMENTS OF NERVOUS TISSUE WHICH SURROUND IT LIKE SHEATHS (pp. 123—127).

However there occur naked axones of considerable length, which likewise are commonly termed (non-medullated) nerve fibers, for instance the fibers of the optic nerve[1] in that part of their course which lies within the retina, also those fibers of the olfactory nerve[1] which arise from the neuro-epithelial cells of the olfactory mucous membrane. In addition within the central nervous system there are portions of medullated nerve fibers whose axones, after their origin from the cell, are non-medullated for a distance which usually is quite short but may be of considerable length.

What were formerly called NERVE FIBERS in the majority of cases are axones surrounded by their special sheaths and are found in the larger nerve trunks, or in the white substance of the central nervous system, or in the nerves and plexuses of the sympathetic system. In such situations the nerve fibers lie pressed closely together and usually run a common course of greater or less length; courses of several centimeters are frequent.

For purposes of description, nerve fibers may be subdivided on the basis of their structure into two large groups: 1. medullated nerve fibers, 2. non-medullated nerve fibers. The former represent in general nerve fibers of the cerebrospinal nervous system, the latter those of the sympathetic system; although within the latter system there do occur some medullated fibers; just as some fibers and even entire nerves of the cerebrospinal system may lack a medullary sheath.

This rule holds good only in the majority of cases, for within the sympathetic nervous system there do occur medullary sheaths which usually are extremely thin; however their number is small, and their presence restricted to particularly long axones. On the other hand within the cerebrospinal system there are some non-medullated fibers, quite apart from young and embryonic fibers lacking the medullary sheaths which they will not receive until some considerable time after birth. But in other cases as well, medullary sheaths may be lacking, *e. g.* the nonmedullated fibers of the optic and olfactory nerves previously mentioned. Moreover the sensory nerve trunks of the cornea carry only non-medullated fibers.

a. Medullated Nerve Fibers

Pl. 15, Fig. 4
Pl. 16, Figs. 8—10
Pl. 17, Figs. 1—7
Pl. 35, Figs. 2, 3

Although the medullated nerve fiber in its structure is really the more complicated type, it will be described first, because it represents by far the most common form of nerve fiber found in the human body.

A medullated nerve fiber lying within the central nervous system is composed of axis cylinder and medullary sheath only; while medullated fibers lying within the peripheral system have a third sheath, the so-called sheath of SCHWANN or neurolemma. Consequently a distinction is made between medullated fibers with neurolemma and those without neurolemma. The former are found in the peripheral nervous system, the nerve trunks and their branches being formed by medullated nerve fibers embedded in connective tissue (p. 174). The latter form the white matter of the central nervous system, in which situation they are embedded in neuroglia. They occur also in greater or less number in the grey matter of the central nervous system, likewise embedded in neuroglia. To this rule there is no exception.

Medullated nerve fibers are almost exactly cylindrical structures with perfectly smooth surfaces.[2] They are often of very considerable length, 50 cm. or more. It must be noted that the fiber is longer than the nerve trunk within which it runs because it is continued without subdividing into the branches of the latter; and even passes beyond the limits of the branches proper.

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[1] Neither of these examples are peripheral nerves.

[2] If, in a preparation, the surface does not appear smooth but is wavy, the condition is an artefact caused by the fiber not being under tension.

The thickness of medullated nerve fibers is highly variable but usually lies between 2 μ and 20 μ. This variable thickness depends upon two factors: 1. the thickness of the axis cylinder, 2. that of the medullary sheath. The neurolemma where present has always the same thickness, which however is very slight (p. 126).

The most important constituent of every nerve fiber is the so-called **axis cylinder**, neuraxone, or neurite. As the first name indicates, it is the central part of the fiber and Pl. 17, Figs. 1-7 as already mentioned represents the axone of the parent cell. The structure of the axis cylinder is characteristic; it is composed of a cylindrical thread of protoplasm (neuroplasm) within which neurofibrils are embedded. The latter show, as in the axone of the nerve cell, an almost exactly parallel and longitudinal arrangement; so that in cross sections of axis cylinders the fibrils appear as fine points, while in longitudinal view the axis cylinder seems to be longitudinally striated. However the neurofibrils divide at very acute angles in their course within the nerve fiber. They seem to be rather uniformly distributed within the neuroplasm, only a thin external zone of the axis cylinder remaining free from fibrils and forming the so-called axolemma.

In form the axis cylinder, like the entire nerve fiber, is almost a true cylinder; only at the nodes of RANVIER (p. 125) is it slightly narrowed. In diameter it varies widely. As a rule, but not invariably, the large nerve cells give rise to axones, that is to say to axis cylinders and thus indirectly to nerve fibers as a whole, that are thicker than those which take origin from small cells. This rule holds almost without exception for cells of the same class. The axis cylinder always represents the thickest part of the nerve fiber. However, most fixing fluids cause the medullary sheath to swell greatly, compressing the axis cylinder which then appears proportionately thin. But this is always an artefact. The diameter of the axis cylinder may vary from 1 μ to 15 μ and the number of neurofibrils from 20 to 100.

When examined in the fresh (living or surviving) condition, the axis cylinder of a nerve fiber appears quite faint and but feebly refractive. The fibrils are not visible without Pl. 17, Fig. 1 the employment of special stains.

The **medullary sheath** surrounds the axis cylinder like a cylindrical tube. Within the central nervous system it covers without interruption the axis cylinder of the medullated nerve fiber in all its extent which is devoid of neurolemma. Within the peripheral nervous system, where the medullated fibers possess a neurolemma, the medullary sheath shows very short interruptions at regular intervals (p. 125). The medullary sheath thus surrounds the axis cylinder and does not lie in the interior of the fiber as its name "medulla" might imply. The thickness of this medullary sheath is highly variable: there are medullated nerve fibers in which it can be recognized only after being stained and by employing very high Pl. 17, Figs. 4—7 magnification. The least thickness possible for the medullary sheath is much less than 1 μ, while on the other hand its greatest thickness may reach 3 μ and even more.

As previously described, the white matter of the spinal cord and brain (including the optic nerve) is formed of medullated nerve fibers, each of which is composed of a centrally placed axis cylinder surrounded by an uninterrupted medullary sheath; while the medullated fibers of the peripheral nerves possess in addition a neurolemmal sheath.

The substance which forms the medullary sheath of medullated nerve fibers is known as myelin. It is a soft and almost fluid substance which has a high refractive index since it consists, for the most part, of lipoids such as cholesterin and lecithin. In addition myelin is doubly refractive. However the whole medullary sheath does not consist of myelin;

there may be demonstrated an additional material which forms an extremely delicate framework for the myelin and can only be shown when the myelin proper is removed by reagents which dissolve fat; *e. g.* by boiling in alcohol. The substance of this framework is termed NEUROKERATIN. It takes the form of delicate threads which permeate the entire medullary sheath and which are very resistant to reagents such as acids and alkalis.

Pl. 17, Fig. 2

Like all lipoid materials the medullary sheath is blackened by osmic acid; but in addition it, or at least its chief constituent, the myelin, is extremely sensitive to reagents. Thus myelin swells, particularly in water, and protrudes as peculiar cloudy structures (so-called myelin formations) at the cut ends of nerve fibers. These formations show indications of concentric layers. Most other reagents, such as the fixing materials commonly used, also cause the medullary sheath to swell; so that in most preparations of tissues (really in all except those which have been fixed by osmic acid) the medullary sheath appears disproportionately thick and the axis cylinder, being compressed by the swollen medullary sheath, seems much thinner than it actually is.

Pl. 16, Figs. 9, 10

When examined in the fresh condition the medullary sheath of the surviving nerve fiber appears to glisten under the microscope as a result of its great refractive power. It appears also to have a double contour, *i. e.* it is bounded by dark lines both within and without. Of these two contour lines the outer is always the heavier. Between the two contour lines the medullary sheath appears to be pale yellowish, a coloring which in general is noticeable only in very thick fibers and those which have a thick medullary sheath. The thinner the fibers become the more closely do the two dark contour lines draw together.

Pl. 35, Figs. 2, 3

The medullary sheath of those fibers which lie beyond the boundaries of the central organs (brain and spinal cord) and which consequently possess neurolemmal sheaths, show at short and regular intervals interruptions which are only a few microns in length. At such places the medullated nerve fiber appears as if constricted for a few microns. These appearances are named **nodes of Ranvier** after their discoverer. The interruption to the medullary sheath is recognized at once under the microscope by the lack of the glistening so characteristic of this layer. For the short distance within which the medulla is lacking the medullated nerve fiber consists of axis cylinder and neurolemma only. These nodes follow at quite regular intervals which however vary somewhat with the thickness of the nerve fiber. In quite thick fibers the intervals measure exactly one millimeter; in thin fibers they are somewhat less (0.8 mm.). In the fine medullary sheaths frequently possessed by especially long fibers of the sympathetic nervous system, the nodes of Ranvier appear to be lacking. Neither neurolemma nor nodes of Ranvier are to be found in fibers within the central nervous system.

Pl. 16, Fig. 8
Pl. 17, Figs. 1, 4

Special methods of treatment, involving the use of certain stains, show in the medullary sheath structures which either are not visible at all in the fresh nerve fiber or are barely indicated. It is extremely questionable whether these pictures correspond to pre-existing structures; this perhaps is even true for the picture of the neurokeratin network. After the employment of many fixing agents (those which contain salts of chromium) which cause the medullary sheath to swell greatly, a radial structure is noticeable in the sheath, *i. e.* there appear in the medulla, fine lines which look like radial septa. Other fixing agents, such as osmic acid, show in the medullary sheath, which is not blackened in all parts by this reagent, delicate, concentric, unstained lines alternating with the blackened zones. In such osmicated nerve fibers there appear peculiar narrow interruptions of the medulla which run obliquely to the surface, the so-called SCHMIDT-LANTERMAN incisures, indications of which are also to be seen upon examination of fresh nerve fibers. The angle between

Pl. 16, Figs. 9, 10
Pl. 35, Figs. 2, 3
Pl. 17, Figs. 4, 5

the incisures and the surface of the fibers varies, as a rule, from 30⁰—60⁰. The incisures follow parallel to one another, at least for a short distance, but may suddenly appear with their direction reversed. The individual segments of the medulla which lie between two such incisures are referred to as cylindo-conic segments. Probably the incisures have to do with the nourishment of the medullary sheath; they are said to be filled with an albuminous material.

Pl. 17, Fig 6

The appearance of these incisures in the medullary sheath is probably connected with the fact that, according to the views of many authors, the medullary sheath is penetrated by protoplasmic processes from the sheath of SCHWANN. It may be represented accordingly that these oblique incisures are filled with delicate prolongations of protoplasm from the neurolemma. It is well recognized that certain methods, *e. g.* staining the medullary sheath in frozen sections, show the substance of the medulla formed into very peculiar funnel or fin-like shapes, so that many authors speak of a medullary spongium. It is extremely difficult to bring these pictures into harmony with those of the framework of neurokeratin, and especially difficult to decide which structures pre-exist in the medullary sheath and which do not.

Other peculiar appearances are seen in the medullated nerve fiber when the latter is treated with solution of silver nitrate. These are the so-called Latin crosses or crosses of RANVIER caused by a blackening of the axis cylinder at the nodes of RANVIER. Since the precipitate of silver at these places lies across the axis of the fiber a cruciform figure results. If the action of the silver nitrate solution goes further successive zones of blackening result; these markings consist of extremely fine granules and are known as the transverse lines of FROMANN.

Pl. 17, Fig. 3
Pl. 16, Figs. 8, 9
Pl. 17, Fig. 1

The outermost layer of the medullated fiber is the **neurolemma** or **sheath of Schwann.** As already related it is lacking in medullated nerve fibers within the brain and spinal cord, in which situations the nodes and other special structures which have been mentioned are also lacking. This sheath is a very thin tubelike structure, whose thickness in the greater part of its course is much less than one micron. Since it is a structure which bears nuclei at definite intervals the sheath of Schwann as a whole must be regarded as a syncytium, one indeed which possesses a remarkably great length and whose form must be regarded as that of a tube with an extremely thin wall.

Pl. 17, Fig. 1

In examination of a fresh nerve fiber the neurolemma is difficult to recognize since it is not only very thin but also has very little refractive power. It is best seen at the nodes of RANVIER where it lies directly upon the axis cylinder and is united to the latter by a kind of cement. It may also be seen if it is artificially raised away from the surface of the medullary sheath, to which otherwise it is firmly adherent. Naturally it is especially evident wherever it bears nuclei.

Pl. 16, Figs. 8, 9
Pl. 16, Fig. 9

These neurolemmal nuclei are found at quite regular intervals. One nucleus occurs in each segment between two nodes of RANVIER (so called interannular segment); moreover it lies exactly in the middle of the segment. The intervals between these nuclei of SCHWANN, as they have been called after their discoverer, are thus exactly as large as are those between the nodes of Ranvier. It is the rule that in two successive segments nuclei shall alternate in their position. The nuclei are usually short ellipses and as a result frequently produce corresponding depressions on the medullary sheath; only in very fine nerve fibers are they greatly flattened. Otherwise they show no marked peculiarities. Surrounding the nuclei there is to be seen a considerable layer of the syncytial cytoplasm of the neurolemma.

As has already been described in connection with nerve cells which lie outside of the central nervous system (p. 118), they too are surrounded by neurolemma. However this pericellular sheath contains more nuclei than do the delicate neurolemmal sheaths of the nerve fibers. A more independent neurolemma with abundant nuclei occurs in connection with many nerve terminations, both of motor and of sensory nerves (see Part B, chapter IV).

The neurolemma of the peripheral nervous system has been compared with the neuroglia of the central system (p. 128), and the two regarded as homologous. It is most highly probable that this is a correct conception, and that neuroglia and neurolemma represent equivalent structures, both of which are derived from the outer germ layer and in the formation of the embryo take origin from the neural tube just as do the nerve cells themselves. The latter (nerve cells proper) proceed from cells known as neuroblasts situated in the neural tube or in the ganglionic ridges; while the mother cells of the neuroglia and of the neurolemma are the so-called spongioblasts found in the same situations.

Peculiarities of structure have been described in the so-called cells of SCHWANN (*i.e.* the nucleated masses of protoplasm midway between two nodes) the significance of which (if any) is as yet uncertain. The view has already been mentioned that the protoplasm of the neurolemma enters into the medullary sheath at the incisures of the latter; in addition granules resembling those which occur in glia cells have been demonstrated in the protoplasm.

b. Non-medullated Nerve Fibers

Apart from the naked axis cylinders of the optic nerve and of the fila olfactoria previously mentioned there are some other non-medullated nerve fibers, *e.g.* in the cornea, which are merely portions of nerve fibers that, for a distance, have lost their medulla. Consequently they consist of axis cylinder and neurolemma and are formed exactly like the medullated portion of the fiber, only the medullary sheath is lacking.

The non-medullated fibers of the sympathetic system known after their discoverer as REMAK'S fibers are essentially different. For within the sympathetic system a large number of nerve fibers remain without medulla throughout the whole or greater part of their length. Naturally, these nerve fibers consist of axis cylinder and neurolemma, but both of these constituents, particularly the neurolemma, differ somewhat from their equivalents in the medullated nerve fibers.[1]

Pl. 16, Fig. 10
Pl. 17, Fig. 8

In the first place as regards diameter the non-medullated fibers of the sympathetic nervous system do not vary as do the medullated fibers. The non-medullated sympathetic nerve fibers are more nearly all of the same thickness, which, considering the lack of medullary sheath, is relatively great. They are only approximately cylindrical structures, the fibers being regularly flattened in one direction and thus forming thick bands of irregular contour. The same is true of the naked axis cylinders mentioned above. In the fibers of the sympathetic system there appears to be a syncytial connection between the axoplasm on the one hand and the neurolemma on the other. For it is not possible to separate the axoplasm from the protoplasm of the sheath of SCHWANN which here contains a disproportionately large number of nuclei. Indeed neurolemmal nuclei are frequently found in the interior of the fibers.

Pl. 16, Fig. 10
Pl. 17, Fig. 8

As mentioned, the neurolemma of these non-medullated fibers contains a greater abundance of nuclei than does that of the medullated fibers. The number of nuclei found at short intervals of about 30—40 μ is several times the number of nuclei in an equal length of medullated fiber. In form the nuclei are invariably elongated, usually indeed they are so long and slender as to recall the nuclei of smooth muscle.

Pl. 17, Fig. 8

As regards the axis cylinder of non-medullated nerve fibers, their neurofibrils are seen more distinctly than are those in the axis cylinders of medullated fibers and they also appear to be of greater diameter. They are easily seen in both cross and longitudinal sections, even when ordinary tissue stains are used. They may be distributed in the axoplasm at uniform distances but more commonly they are arranged in groups, giving the impression that this variety of non-medullated nerve fiber actually consists of small groups of axis cylinders surrounded by neurolemma. This would explain the presence of neurolemmal nuclei in the interior of the fiber. As mentioned, the non-medullated nerve fibers vary in diameter within rather narrow limits (7—12 μ).

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[1] As already noted there are many MEDULLATED nerve fibers within the sympathetic system; however as a rule their medullary sheaths are extremely thin. Sympathetic nerve fibers with thick medullary sheath can scarcely be said to occur.

While nerves which consist altogether, or largely, of medullated fibers appear white (and the regions of the brain and spinal cord which consist of massed medullated nerve fibers show the same color), the nerve trunks (usually small) which consist altogether, or chiefly, of non-medullated fibers appear grey; which consequently is the usual color of nerves of the sympathetic system. For the extremely thin medullary sheaths, which many of the latter fibers possess, exercise little or no influence on the color because of the extreme thinness of the medulla. The white color is only produced when considerable numbers of medullated nerve fibers lie close together. Thus the grey matter of the brain and spinal cord retains its grey color, although numerous medullated fibers (p. 160) lie within it.

3. The Supporting Substance of Nervous Tissue. Neuroglia

Within the organs of the central nervous system, brain and spinal cord, the nervous elements, the neurones (cells, fibers and telodendria), are not embedded in connective tissue but have a peculiar supporting substance, the NEUROGLIA, which is found only in these situations. It differs markedly from connective tissue and is not derived from the Pl. 18 mesoderm but is of ectodermal origin.

The wall of the embryonic neural tube at first consists of quite similar epithelial cells which later become differentiated into two types. One of these types very soon relinquishes its epithelial character and its cells are then known as neuroblasts because they are the antecedents of the later nerve cells, or neurones. The cells of the other type retain their epithelial character somewhat longer, or even permanently, and bear the name of spongioblasts. These cells are the antecedents of the future neuroglia. From this mode of origin it is clear that neuroglia is a cellular tissue; even where fibrous elements enter into its structure they have been produced by the glia cells proper.

Pl. 18, Fig. 1 Neuroglia appears in a great variety of forms. There are, so to speak, more highly Pl. 32, Fig. 5 differentiated forms of glia cells and others which in characteristics stand nearer to the embryonic spongioblasts. The so-called **ependymal glia** belongs to the latter group (p. 110). The ependyma lines the cavities of the brain and spinal cord and when ordinary staining methods are employed its cells give the impression of a simple cubical or columnar epithelium with a kind of cuticular border on its free surface replacing the cilia of its Pl. 18, Fig. 1 embryonic condition. When special staining methods are used it may be shown that from the base of each of these cells there proceeds a glial fiber, the so-called ependyma fiber, which after a short course branches and along with branches of neighboring fibers forms beneath the epithelium a glial fiber layer of greater or less thickness. Such layers, Pl. 32, Fig. 5 formed chiefly or entirely of glial fibers, are named substantiae gelatinosae. Thus the ependymal glia of the spinal cord forms the substantia gelatinosa centralis around the central canal of the organ (p. 162). In the embryonic condition the ependymal fibers traverse the entire thickness of the wall of the spinal cord.

The most common form in which the cellular elements of the neuroglia occur is that Pl. 18, Figs. 1—4 of the so-called **astrocytes** (of DEITERS). They form the greater part of the glial elements of the white matter of brain and spinal cord; *i. e.* of the parts of these organs which are devoid of nerve cells and which are composed of medullated nerve fibers only. They also predominate over the other elements of the neuroglia in the grey matter; *i. e.* of the parts of brain and spinal cord in which the nerve cells are present. It is customary to distinguish two types of glia cells: those with long and those with short rays. The latter are cells composed chiefly of protoplasm and marked by the possession of greatly branched processes, but containing few fibrous elements; while the forms with long rays contain numerous fibers.

The astrocytes of the neuroglia are cells with abundant protoplasm and more or less flattened, spherical or ellipsoid nuclei, which in rare cases show slightly polymorphous forms. The nucleus always stands out clearly and, when ordinary stains are used, as a rule only the nuclei of the glia cells can be seen distinctly. They differ from the nuclei of nerve cells in lacking the nucleolus characteristic of the latter, and in having a more stoutly formed chromatin network; for which reason they stain more intensely than do the nuclei of the nerve cells. The cell body may, as is typical for the short-rayed forms, possess branches which according to circumstances may ramify very extensively or, as is typical for the long-rayed forms, may show but few branches. In addition the protoplasm of the astrocytes contains highly variable numbers of fibrous inclusions, the **glia fibers,** Pl. 18, Figs. 5, 7
which by the employment of appropriate methods may be stained selectively. They are fine, bristle-like, fibrous differentiations which often reach considerable length and are unbranched. They traverse the body of the cell, and thus for a short distance are intracellular; but when, as is usually the case, they are of considerable length their free ends pass far beyond the territory of the cell, *i. e.* beyond the boundary of the part of the protoplasm which has not been differentiated into fibers. In the short-rayed forms these glia fibers are few and short; but in the long-rayed forms they are long and numerous and produce the peculiar appearance of this type of astrocyte.

The SHORT-RAYED ASTROCYTES are thus glial elements which are poor in fibers and which are characterized by short processes dividing repeatedly in a dichotomous manner. They are completely absent from the white matter but are found in abundance in the Pl. 18, Figs. 3, 4
grey matter, which on the whole contains the greater quantity of neuroglia. Within the grey matter they lie preferably near blood capillaries, indeed as a rule they even send to the vessel some processes which terminate on the wall of the vessel itself (really on the membrana limitans perivascularis) in slightly thickened ends, the so-called glial footplates.

On the other hand the LONG-RAYED ASTROCYTES contain numerous fibers, the cell body being traversed by a greater or less number of true glia fibers. The fibers are of very Pl. 18, Figs. 2, 7
considerable length and in Golgi impregnations appear as long, fine, unbranched extensions of the cell passing beyond the territory of the cell body. According as the fibers traverse the body of the cell in parallel courses, or run through it in all directions, they radiate from a few regions or (more frequently) from all sides. Often the glia fibers run parallel to one another through the body of the cell and emerge from it at opposite poles. As the glia fibers leave the body of the cell they are invariably covered for some distance by protoplasm; thus outside of the cell body in the narrow sense, they still lie, at least for a short distance, within its protoplasm. Beside being present in the grey matter these long-rayed forms of astrocytes are to be noted as occuring in the white matter where they represent the rather scanty glial elements proper.

The glia fibers, which occur in relatively small numbers in the short-rayed group of astrocytes, are abundantly present in those with long rays. They are extensively interwoven in order to form the bed for the neurones; particularly for the cell bodies. This framework of neuroglia is known as the GLIOPIL and forms the basis of support for the neuropil (p. 121). Pl. 18, Fig. 6

In the immediate neighborhood of the larger forms of nerve cells, there are regularly observed cellular glial elements which have a most intimate relationship to the nerve cells in question. These glia cells consequently are termed SATELLITE CELLS. There are two Pl. 16, Fig. 7
different forms of glia cells, which may occur as satellites of nerve cells. Probably the greater number of satellites belong to the so-called OLIGODENDROGLIA, while the minority of the group are to be included among the so-called HORTEGA CELLS or MICROGLIA. Both these

types of neuroglia cells have one point in common; they do not develop glia fibers. Both are glia cells which differ markedly from the ordinary types of astrocytes. The **oligodendroglia** consists of proportionately large cells which, because of the extreme fineness of their processes give the impression of being epithelioid cells; the more so since frequently only special methods will succeed in staining the processes at all. The body of the cell varies greatly in form, being irregularly polyhedral, pear-shaped, or almost cubical. The nucleus is spherical and clear (vesicular), and is of large or medium size. A few processes which usually are very fine and only moderately branched emerge from the cell body. As already mentioned, the cells form satellites, for instance of the large pyramidal cells of the cerebral cortex. In addition, oligodendroglia have a relation to blood vessels which is merely one of proximity. Just as in the case of the satellites it is the body of the cell which is applied to the nerve cell, so here it is not the processes, as would be the case with astrocytes, which are connected with the wall of the vessel, but it is body of the cell itself. Cells of the oligodendroglia may occupy isolated positions and may also be observed, particularly in the white matter, to be arranged in groups and even in rows.

The **Hortega cells,** as they are best named, (from their discoverer, del Rio-Hortega) Pl. 18, Fig. 8 in contrast to the oligodendroglia, are little glial elements in which the cell body proper is of noticeably small size (microglia). A thin zone of protoplasm surrounds the dark nucleus which is correspondingly small but is usually rather elongated or irregular, often appearing bent. The body of the Hortega cell sends out only a small number of processes which are rather stout as they emerge from the cell, but then break up into numerous and extremely fine branches, slender lateral twigs coming off from the larger branches almost at right angles. The outline of the cell varies according to the number of branches, which as mentioned, is always small; *e. g.* two branches produce a bipolar cell.

In general this type of cell is uniformly distributed throughout the central nervous system but is most abundant where astrocytes are most numerous, *i. e.* in the grey matter; so that the microglia doubtless participates in forming the general gliopil. It has already been mentioned that its cells form one variety of the satellite cells, the chief cell being grasped either by the body of the satellite cell or by its processes. They are also applied to the blood vessels, the cell body itself usually being much elongated and in contact with vessel.

The relations of the Hortega cells in particular, show that the neuroglia has not only a supporting function for the nervous elements, but that it also plays an important role in their nourishment. The transport of nourishment and of waste products between the blood vessels and the nervous elements is accomplished through the neuroglia and it is the Hortega cells in particular which conduct this transport (iron, lipoids, glycogen). They act as true storage cells.

B. Microscopic Anatomy of the Organs

1. Organs of the Skeletal System

The organs of the skeletal system comprise the bones and their articular and ligamentous connections.

In the living condition the bones consist not only of bone tissue (p. 78) which forms their outstanding constituent, but also of soft parts. The constituents of a bone, consequently are:

1. bone, 2. periosteum, 3. the blood vessels and nerves of the bone, 4. marrow, 5. the articular cartilages.

Bone

Pls. 19, 20 The chief mass of the bones as a whole, at least of all the larger elements of the skeleton, consists of **bone, substantia ossea.** This consists of bone tissue arranged in a definite manner. It has already been mentioned in describing bone tissue (p. 78) that there are different forms in which this variety of tissue occurs, depending essentially upon the condition of development of the skeletal part in question; however in some parts of an adult bone there may yet be remnants of the juvenile type of bone substance. The following description of a typical bone considers it as an organ formed of that variety of bone substance which predominates in by far the greater number of the bones of the skeleton, that is to say, of LAMELLAR BONE. Spongy bone,[1] *substantia ossea spongiosa*, is a very simple lamellar bone tissue in which the blood vessels are arranged without reference to the lamellae. The most slender trabeculae of the spongiosa frequently do not show distinct lamellae. Compact bone, *substantia ossea compacta*, on the other hand shows a more developed and at the same time a more regular lamellar arrangement which is essentially determined by the course through the bone of the canals which lodge the blood vessels. While the trabeculae of spongy bone are devoid of all blood vessels, compact bone is permeated by a wide-meshed vascular network. The canals in the compact bone, in which lie the blood vessels of medium and smaller size, are known as HAVERSIAN CANALS. In bones with stout, compact walls, *i. e.* in tubular bones, they run parallel to the long axis of the bone and corresponding to the behavior of the blood vessels, they show dichotomous branching and anastomoses. Their diameter usually measures 20—100 μ, yet there do occur canals which are only half as large, and others of many times this diameter (10—400 μ). The caliber varies according as they contain larger or smaller arteries (or veins), or capillaries.

Pl. 21, Fig. 1 The Haversian canals thus contain some of the soft parts of the bone; consequently in the picture of a ground section of bone they are empty, but in that of decalcified bone they contain, as mentioned, blood vessels (often artery and vein lying side by side as well as capillaries, see page 134). Those of larger caliber invariably contain also a certain amount of marrow. Scattered marrow cells are also found in canals of medium size, the vessels being separated from the wall of bone by a small amount of connective tissue rich in cells.

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[1] Concerning the distribution of compact and spongy bone see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. I.

For the most part of the systems of lamellae of compact bone surround these canals
Pl. 10, Fig. 3 in concentric arrangement. These lamellae are termed HAVERSIAN LAMELLAE or special
Pl. 20, Fig. 1 lamellae. The number of lamellae surrounding an Haversian canal usually varies from 8—15, the extremes are 5 and 20. The lamellae may reach a thickness of 7—10 μ. They are not invariably complete rings but often describe only two-thirds or three-quarters of a ring, and then pass over into neighboring lamellae. The canals of medium caliber commonly have the greater number of lamellae, those of large diameter are often surrounded by remarkably few lamellae. The lacunae of the bone, with their contained cells (p. 78), lie in the lamellae, just one layer in each lamella. The lacunae of the innermost row are connected with the Haversian canal itself by their canaliculi. The lacunae are so placed in the lamellae that the long axis of the lacuna is parallel to the long axis of the canal; and the lacunae of neighboring lamellae usually alternate. The direction of the fibrils within a lamella is variable, often they lie at right angles to one another in two adjacent Haversian lamellae; for instance, in one lamella they are concentric with the canal, and in the next lamella are parallel to the long axis of the latter. However, the direction of fibrils in neighboring lamellae may be the same. The bone capsules and the narrow zones of bone matrix immediately surrounding the canals (p. 79) and also the so-called cement lines (see below) are devoid of fibrils.

In addition to the Haversian lamellae two other varieties of lamellae are to be distinguished in compact bone; first, those which run parallel courses upon the inner and outer surfaces of the bone, the so-called internal and external GROUND LAMELLAE, general lamellae, or superficial lamellae. Of these, the external lamellae formed by the periosteum are commonly much stouter and more regular than are the internal. Second, in the intervals between the systems of Haversian lamellae, there is found a system of lamellae of irregular wedge-shaped form, not connected with the vascular canals; these are the INTERSTITIAL LAMELLAE. These lamellae are clearly formed in situations where the neighboring Haversian systems are not in immediate contact. There is no regularity in the position of the lacunae within them; while in the external ground lamellae the lacunae lie with their surfaces exactly parallel to the surfaces of the lamellae. Many interstitial lamellae are derived from partly resorbed Haversian systems, and are those sectors of the latter which have not been removed. Tangential sections of Haversian lamellae may often
Pl. 20, Fig. 1 simulate interstitial lamellae. The individual lamellae are firmly united to one another by a small quantity of so-called cement, *i. e.* matrix which is free from fibrils. This cement appears especially abundant at the boundary of the individual systems of lamellae, which are separated by broad lines of cement.[1] In addition to the Haversian canals, there are found in compact bone still other vascular canals which usually come from beneath the periosteum, and in variable number and direction penetrate the external lamellae
Pl. 19, Figs. 1, 4 without influencing the arrangement of the latter. In rare cases they extend outward from the marrow cavity. They pass without demarcation into the Haversian canals. Their number is highly variable and usually their diameter is small (10—30 μ). They are termed the canals of VOLKMANN and are common in the mandible. In other bones

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[1] Between the individual systems of lamellae there are broad and distinct cement lines which frequently are noticeable through their peculiar power of staining. In addition there are within the Haversian systems similar lines of cement, running concentrically about the canal and staining almost exactly like those above mentioned.

they are much less frequent. Their origin is probably to be referred to the processes of resorption.

Slender bundles of connective tissue fibrils (up to 30 μ), often containing elastic fibers, are frequently found to proceed from the periosteum and penetrate the external lamellae, and to some extent also the lamellae of the neighboring interstitial systems. They pass through the lamellae in transverse or oblique directions and promote a firmer union between bone and periosteum. They are known as SHARPEY'S FIBERS and are uniformly present in many bones. They are most common during youth, and in bones of connective-tissue origin (membrane bones); that is to say, in the bones of the skull, particularly at the borders of the sutures and in the reticulated bone (p. 80) in which a lamellar structure is wanting. They never occur in the Haversian lamellae or in the internal ground lamellae.

Pl. 20, Fig. 5

In most bones, in addition to the compact and spongy bone of lamellar structure, there is found also the coarse-fibered tissue of reticulated bone, particularly at the places where tendons or ligaments are united to the bone, and also at the sutures of the skull. Concerning the features of bone as it adjoins the articular cartilages see below.

The **periosteum** is a thin but strong connective-tissue membrane in which there may be distinguished two rather poorly defined layers. The outer contains numerous blood vessels and nerves, and a great abundance of fibers, which usually, but not invariably, run in a longitudinal direction. For the most part these are collagenous fibers but some elastic fibers are also intermingled. The inner layer of the periosteum on the other hand is poor in blood vessels, but contains an abundance of elastic fibers (so-called FIBRO-ELASTICA) and a proportionately great number of connective tissue cells. On its inner surface next to the bone there may lie osteoblasts, and in the case of growing bone their presence in this situation is invariable. The periosteum is especially thick in situations where a bone lies immediately beneath the skin, and is much weaker where the bone is covered by muscle. Usually the periosteum is but loosely attached to the bone so that it may readily be stripped off; where it is firmly attached the more intimate union is brought about by the fibers of Sharpey.

Pl. 19, Figs. 3, 4
Pl. 20, Fig. 5

The **articular cartilage, cartilago articularis,** is usually a thin layer of hyaline cartilage covering the articular ends of bones, its thickness varying from one-quarter of a millimeter to four millimeters (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. I). It is the last remnant of the original embryonic cartilaginous skeleton which has gradually been replaced by bone (p. 136). As a result the zone of transition between the articular cartilage and the bone shows the phenomena of calcification, *i. e.* the part of the articular cartilage next to the bone is calcified. Then follows a zone in which the fibrillar structure of the cartilage is especially distinct and the cartilage cells, surrounded by stout capsules, are formed into groups and rows perpendicular to the surface. In the middle the cartilage cells are rounded, and in the outer layer they are flattened in a direction parallel to the surface. The articular cartilages as a rule have no covering of perichondrium, with the exception that in many joints their margins are partly covered by a layer of connective tissue as by a perichondrium. The boundary between the articular cartilage and the epiphyseal bone is never smooth and even (p. 139).

The BLOOD VESSELS of a bone may be divided into those which enter its substance from the periosteum, and the *arteriae nutriceae* which usually pass into the marrow through the nutrient canals. In the adult the nutrient arteries are less developed than in youth, frequently they are completely atrophied. This is connected with the fact that they are primarily devoted to the red bone marrow and when the latter is transformed into yellow marrow, which contains few vessels, the nutrient arteries diminish in caliber. The vessels of the marrow and the inner parts of the bone are derived from the nutrient arteries; those of the outer parts from the periosteum. The branches of the periosteal vessels use the canals of Volkmann and of Havers in their course within the bone, and pass into capillaries in the marrow. The veins of the marrow have extremely thin walls which only apparently show imperfections. The veins in the Haversian canals have no trace of either musculature or of valves and as a result their walls are exceptionally thin.

These characteristics of the vessels of the bone are essentially true only for the diaphyses of the tubular bones, in which it is to be noted that apart from the numerous anastomoses of the arteries and veins of the Haversian canals, capillaries are also present. This is related to the fact, already mentioned, that these canals contain a greater or less quantity of red bone marrow.

The epiphyses of the long tubular bones show peculiarities in their vascular supply; for in accordance with their development and ossification (p. 139) they have special vessels which are quite independent of those of the diaphysis. So that, apart from a very few anastomoses across the epiphyseal line, the latter forms a sharp separation between the two systems of vessels. The small arteries in the epiphyses form an extensive anastomotic network which shows especially well developed arcades close beneath the articular cartilage.

True LYMPHATIC VESSELS do not appear to be present in bone proper but do occur in the periosteum and, according to some authors, in the Haversian canals as well. NERVES are present in bone, not merely in the periosteum where blood vessels and Vater-Pacinian corpuscles are common, but also in the marrow. They accompany the vessels in the Haversian canals but have not been followed into the bone substance proper. Not only are vaso-motor nerves present from the sympathetic system, but cerebro-spinal fibers may also be found.

In addition to covering the articular ends of bones (p. 133) **cartilage** is to be found in some other restricted situations in the adult skeleton, chiefly as the CARTILAGES OF RIBS. These consist of hyaline cartilage with asbestiform degeneration of the matrix (p. 75), surrounded by a membrane, the perichondrium, rich in elastic fibers. The innermost layer of the perichondrium passes almost without demarcation into the outer layer of the cartilage, which consists of markedly flattened cells and very little matrix.

Bone Marrow, *medulla ossium*

Pl. 11, Figs. 18–20
Pl. 21, Fig. 1

In the adult body, two varieties of marrow are found: red marrow, *medulla ossium rubra* and yellow marrow, *medulla ossium flava*. In childhood all the marrow is of the red variety; in the embryonic state only an antecedent of marrow, the so-called lymphatic marrow, is to be found. In old age, on the other hand, there appears still another form, the so-called gelatinous marrow.

The two varieties of adult marrow are so distributed that the large marrow cavities of the tubular bones invariably contain only the yellow variety, which also enters to some extent into the smaller marrow spaces between the trabeculae of the spongy bone in the articular extremities. In the latter situations it partly replaces the red marrow. In spongy bone the marrow is predominantly of the red variety, and this is also usually the case in the proximal epiphyses of the femur and of the humerus. In addition to occupying the spaces of spongy bone, red marrow is to be found in all the larger Haversian canals and in many of those of medium size.

YELLOW marrow is adipose tissue. It is formed from the red marrow originally present as its reticulum cells are converted into true fat cells by the ordinary process of storing up fat. The so-called gelatinous marrow which is formed from the yellow, particularly in old age, represents an atrophic stage.

Pl. 11, Fig. 18 RED marrow, on the other hand, represents a modified lymphatic tissue in which, beside megakaryocytic giant cells, there are present the antecedent cells from which the granular leucocytes arise. In addition it is the birthplace of the erythrocytes, but only under normal conditions. The detailed account of these, as well as of the structural elements of the marrow has already been given (p. 91). The red bone marrow owes its color to the fact that the red blood corpuscles are formed within it. Since as life goes on, considerable portions of the red marrow of youth are transformed into the yellow variety (adipose tissue), and since this process does not entirely cease even in old age, there are always to be found within red marrow, a number of fat cells, either isolated or in small groups.

As has already been mentioned marrow, at least the red variety, is very rich in blood vessels. Yellow marrow, as is always the case with adipose tissue, contains very few. A close capillary network from the finest branches of the nutrient arteries is everywhere present in the marrow. The venous capillaries of the red marrow, so important for the formation of blood, pass without sharp boundaries into small, thin walled veins. The latter, as well as the venous capillaries, are dilated to form sinusoids and have extremely thin walls. Lymphatic vessels are probably wanting in marrow. The nerves have already been described.

Appendix: The Development of Bones

Although an account of the development of bones lies properly within the field of embryology, yet the general phenomena of their development will be treated here, just as in the account of bone tissue, its histogenesis was discussed. The reasons why the phenomena of the development of bones should be treated in this book are two; first, because the process of the formation of the bones has advanced to only a small extent during intra-uterine life; and second, because new formation of bone and the phenomena of the resorption of bone are to be observed throughout almost the entire life.

According to the manner of their development the bones of man, and of most other vertebrates, fall into two classes; first, those which are preformed in cartilage; and second, membrane bones, *i. e.* bones which are derived by direct ossification of embryonic connective tissue (see text books of embryology and Sobotta-McMurrich, Atlas of Human Anatomy, Vol. I). In principle, the formation of the bony substance, *i.e.* the histogenesis of bone, is the same in both classes; but the manner in which the skeletal part in question is formed, until at last it appears as a complete bone, is a decidedly different process in the two cases.

The Development of "Cartilage" Bones

The principle difference in the modes of development of the two classes of bone lies in this: skeletal elements preformed in cartilage are not formed by direct transformations of existing cartilage into bone; in general, that is not possible (p. 78); while the embryonic connective tissue does become directly transformed into bone. But, apart from exceptions, such transformation cannot occur in a highly and finally differentiated tissue such as cartilage. As a result the replacement of a cartilagenous skeletal part by one of bone can only proceed as the cartilage of the primary skeletal part is removed; only then can bone tissue appear in the place of cartilage. But this process is completed very gradually (see references previously given). Thus it begins early in the third month of embryonic life and does not terminate until long after puberty. Here, only the general processes of ossification in the cartilagenous skeleton will be discussed.

Pl. 21, Figs. 2—5
Pl. 22, Figs. 1—4

Since the great majority of the bones of the skeleton are preformed in cartilage the endochondral mode of the development of bone is by far the most common and consequently will be described first. It will appear that two processes are here running side by side, both leading to the formation of the bone, both proceeding concurrently, but only one of them providing for the replacement of cartilage by bone. One of the processes is known as perichondral (periosteal is not so good a name at this stage) ossification because it proceeds from the perichondrium of the cartilage concerned. The other is termed endochondral ossification, because through it bone appears in the place of cartilage which has been removed. In both processes the manner of the formation of the bone tissue, *i. e.* its true histogenesis, is the same (this applies also to membrane bones); however in the microscopic picture endochondral bone appears quite different from that formed by the perichondrium, so that the one may be easily distinguished from the other.

1. Endochondral Ossification

The formation of perichondral bone slightly preceeds that of the endochondral variety, Pl. 21. Figs. 2–4 for the first trace of it is already visible (p. 137) when those changes may be recognized in the embryonic cartilage which precede the disappearance of the latter. It is noteworthy that the soft cartilage does not dissolve but becomes calcified previous to its disappearance. These processes are best studied in those parts of the embryonic skeleton which are the antecedents of the future long (tubular) bones. Such parts are solid cartilage without central marrow cavity and without any blood vessels; on the whole they possess already in miniature, the form of the later bones. Calcification (p. 76) begins in the very centre of the cartilage and consists in the deposition in the matrix of salts of calcium in a very finely divided state. The matrix thus becomes hard and changes its affinity for basic dyes such as haematoxylin. While the uncalcified matrix stains only moderately well, that which has been calcified makes an extremely firm combination with the haematoxylin, so that it appears dark bluish violet in preparations made with this dye. Because of its deep stain even small remnants of calcified matrix are recognizable after the cartilage as a whole has disappeared. But, besides the deposition of salts of calcium, changes in the cells and in their lacunae are taking place in the calcifying cartilage. The first appearance to be observed in the cells is that in place of the irregular arrangement which obtains in the uncalcified cartilage, the cells at the border of the zone where calcification is beginning now typically become arranged in longitudinal rows, at the same time increasing in size and becoming flattened in a direction transverse to the long axis of the skeletal part. Proceeding further towards the centre of the piece of cartilage, *i. e.* towards the point where calcification is beginning, it is seen that the cells are further increasing in size and particularly that the lacunae are becoming enlarged, so that in a longitudinal section, the individual cavities are separated from one another only by thin walls of calcified matrix which Pl. 21. Fig. 3 look like the rungs of a ladder. Stouter bars of matrix separate the individual rows. At the same time the cells become greatly altered (perhaps through swelling); their nuclei become indistinct and the impression is given that the cells have been destroyed (p. 137).

Only now is the calcified cartilage ripe for its dissolution, which follows immediately. Blood vessels enter into the zone of calcified cartilage; these arise from the perichondrium but their path into the calcified cartilage is no longer open because of the girdle of perichondral bone which has been deposited about this part of the cartilage. They must needs break through this girdle, the point of entrance corresponding to the future foramen (canalis) nutriceum. Now begins the process of removal which is perhaps, in part, a direct chondrolysis on the part of the blood vessels (?); but the chief part is effected by polykaryocytic osteoclasts (p. 81). These are just as able here to accomplish the removal of calcified cartilage matrix (chondroclasts) as they are able elsewhere to remove calcified bone. Accompanying the blood vessels are undifferentiated, embryonic, connective-tissue cells, primary lymphocytes, and osteoblasts, all of which occupy the cavities that are constantly increasing in size within the calcified cartilage.

As the cartilage matrix is removed there is formed in the previously solid embryonic Pl. 21. Fig. 3 skeletal part a cavity, the primary marrow cavity, which steadily grows larger. This cavity has very irregular boundaries, for the removal of the calcified cartilage matrix does not proceed uniformly since the thin walls between the enlarged cartilage lacunae naturally are broken down earlier than the stouter longitudinal walls which separate the rows of cartilage cells. As a result the longitudinal walls which are completely calcified, and which show short lateral teeth (the remnants of the transverse walls), project more or less deeply into the primary marrow cavity.

Pl. 22, Figs. 1, 2

Of the cells which enter the primary marrow cavity with the blood vessels, the primary lymphocytes become the cells of the primary marrow; while the indifferent cells of the mesenchyme form the reticulum. The osteoblasts very soon enter upon their activity, forming the endochondral bone. The question of what happens to the cartilage cells after the rupture of their enlarged lacunae is not settled beyond doubt. Probably they disintegrate, since for some time they have appeared moribund. However some hold the view that, being set free, they become again indifferent mesenchyme or connective tissue cells and participate in formation of the primary marrow.

The osteoblasts having entered the primary marrow cavity apply themselves to the remains of the calcified cartilage matrix (see above) and deposit on the latter a layer of young bone, which at first is very thin and is devoid of cells, but which gradually becomes thicker, at the same time enclosing some of the osteoblasts which thus become bone cells (p. 81). This young endochondral bone never attains great thickness. The trabeculae of cartilage matrix are surrounded on all sides by this young bone and at last are completely encased by it; later they in their turn, will be destroyed by the activity of the osteoclasts. ENDOCHONDRAL BONE IS THUS ALWAYS TO BE RECOGNIZED BY THE PRESENCE IN ITS INTERIOR OF MORE OR LESS IRREGULAR REMNANTS OF CALCIFIED CARTILAGE MATRIX WHICH ARE MOSTLY JAGGED IN OUTLINE AND WHICH STAIN DARK BLUISH VIOLET WITH HAEMATOXYLIN.

Pl. 22, Figs. 1—4

When calcification begins in the middle of a cartilaginous element of the skeleton, in a short time the latter appears slightly enlarged at the site of calcification. However the uncalcified portion of the cartilage continues to increase while growth of the calcified cartilage is excluded. As a result, soon after calcification occurs, the cartilaginous skeletal part appears narrowed at the site of calcification. On the other hand, it is just in this narrowed region that the girdle of young perichondral bone is formed; so that on the whole, partly in cartilage, partly in bone, the skeletal element corresponds roughly to the form of the completed bone.

Pl. 21, Fig. 2

Pl. 21, Fig. 3

The marrow cavity when first formed is small, but as the skeletal part grows, it naturally increases in size. This increase can take place only by the further resorption of previously formed endochondral bone (along with the included remains of cartilage matrix), accompanied by a continual advance of the process of calcification towards the articular ends of the cartilage, with subsequent rupture of the lacunae, etc. The older the embryo and the larger the skeletal part, the greater is the increase in size of the marrow cavity; so that soon a single central cavity is formed filled with primary marrow. Calcified trabeculae of matrix with their covering of endochondral bone project into it only at its ends; its central parts are quite free from such.

Pl. 22, Fig. 1

As is well known, this process of the removal of the embryonic cartilage, which begins relatively early in embryonic life, comes to a halt in the region of the future epiphyseal line of long bones; so that almost without exception the epiphysis remains purely cartilaginous until birth, and often indeed for a long time afterward. In time there will occur in it the provisional calcification, the removal of cartilage and the formation of a separate centre of ossification (see p. 139; textbooks of embryology, and Sobotta-McMurrich, Atlas of Human Anatomy, Vol. I.).

2. Perichondral Ossification

As already indicated, the formation of perichondral bone begins when the first traces of calcification show within the cartilage. In contrast to the endochondral bone which forms within the skeletal part the formation of perichondral bone proceeds externally. As the name shows it is bone formed by the perichondrium, and formed on its inner surface, next to the calcified cartilage. This inner layer of the perichondrium has aptly been referred to as the cambium layer. With the calcification of the cartilage the original function of the

Pl. 21, Figs. 2—4

Pl. 22, Figs. 1, 2, 4

perichondrium, particularly as regards growth of the cartilage, ceases. It now takes up a new task, that of forming a shell of bone around the calcified portion of the embryonic skeletal part, and thus becomes the periosteum.

On the inner surface of the membrane there are seen distinctly the osteoblasts (p. 81) so characteristic of the formation of bone. They secrete upon the surface of the calcified cartilage a layer of young bone, which at first is very thin and devoid of cells, but which gradually becomes thicker and then encloses cells. This young bone corresponds exactly in extent to the calcified cartilage which it surrounds as with a girdle or cuff. As the zone of calcification increases, that is to say, as the removal of cartilage extends further and further, the girdle becomes elongated but is always thickest around the middle where it was first formed. In this region also it eventually forms the boundary of the marrow cavity, the cartilage having disappeared. During embryonic life the mass of endochondral bone (p. 139) is considerably greater than that of bone formed by the perichondrium; so that the young marrow cavities of the anlagen of the long bones of a five months embryo have already a tolerably thick wall of perichondral bone, which becomes gradually thinner towards the articular ends.

But the embryonic bone naturally grows not only in length but also in thickness, which in turn permits increase in the width of the marrow cavity. Thus in young perichondral bone there must be recognized processes of resorption from within which lead to enlargement of the marrow cavity; while from without additional young bone is deposited, so that the girdle of bone expands and does not become diminished in thickness. The re-
Pl. 22, Fig. 4 sorption is effected through the activity of osteoclasts. Very soon after the girdle of bone has attained a certain thickness, the young bone is no longer applied to its outer surface in compact layers, but in the form of separate trabeculae and lamellae. These are connected with one another and continue their growth; so that the periosteal girdle is not smooth on its outer surface but shows numerous open sinuses. The blood vessels lie within these sinuses and thus become surrounded by bone, so that they soon lie in cavities enclosed on all sides; cavities which at first are much larger in diameter than are the blood vessels and whose inner surface is lined by osteoblasts. Through the activity of the latter the cavities steadily become narrower until finally they are reduced to the diameter of an Haversian canal; for such is the mode of formation of the latter. After being released from their function of forming bone, the osteoblasts probably revert to the condition of indifferent connective-tissue cells, or form the marrow cells of the Haversian canal. Through these processes the bone of the periosteal sleeve takes on more and more the character of the final bone, but it consists of reticulated bone only (p. 139); the formation of lamellae does not set in until decidedly later (p. 139).

As already mentioned, the sleeve of periosteal bone is thickest at the site where it first appeared. Towards its ends it becomes noticeably thinner; and as a very thin lamella of bone it extends over the calcifying cartilage, reaching to, or even beyond, the limits of that part of the cartilage which has not as yet become calcified.

The Development of Bone in Skeletal Elements Which Are Not Preformed in Cartilage

Pl. 21, Fig. 5 In the anlagen of the flat bones and portions of bones which share in forming the roof
Pl. 22, Fig. 5 of the cranium, and also in the anlagen of most of the bones of the face, the formation of bone results from a direct ossification of the embryonic connective tissue, as for instance, in the so-called membraneous primordial cranium. This process in principle does not

differ from the formation of perichondral bone in the anlagen of the tubular bones; here also osteoblasts secrete bone matrix which takes up salts of calcium and at first is free from cells. Then, in a similar fashion as in the skeletal parts which are preformed in cartilage, osteoblasts become surrounded by young bone matrix and thus become bone cells (p. 79). Young bone trabeculae of this kind are first formed at the true center of ossification, and at once show an inclination to join and anastomose. From this early nucleus of bone the process of ossification extends into the surrounding areas; usually by means of radial and anastomosing trabeculae which form extensive flat networks with blood vessels lying in the meshes. These spaces are then gradually transformed into Haversian canals by the action of osteoblasts, in the same manner as described above. When the flat anlagen of the membrane bones have reached a certain size they begin again, in the region of the first nucleus of the bone, to thicken by means of trabeculae which form in other planes, but which are connected with those previously developed. The trabeculae of bone, which at first are slender, become thicker on all surfaces because of the uninterrupted covering of osteoblasts which they bear. On the other hand, resorption, brought about by osteoclasts, is soon recognizable. For as a whole the young bone is in the process of formation and naturally must bear the proper proportion to the growth of the head and in particular must afford room for the rapidly growing brain. Consequently, not only during embryonic life, but also during the whole period of the growth of the skull in childhood, extensive processes of resorption are to be observed on the inner surface of the flat cranial bones, offset by apposition of bone to the outer surface.

Pl. 22. Fig. 3

Post-embryonic Phenomena of Ossification

Attention has already been directed to the fact that the different forms in which embryonic bone makes its appearence have not, by the time of birth, led to the complete replacement of the primary cartilaginous skeleton by bone; but that the embryonic processes of cartilage removal etc. continue for a long time after birth. At the time of birth the articular ends of the anlagen of the long bones are almost without exception purely cartilaginous. In these cartilaginous ends new centers of ossification are formed, the epiphyseal centers (see text books of embryology and Sobotta-McMurrich, Atlas of Human Anatomy, Vol I). Corresponding processes occur during the ossification of the short and flat bones. Fundamentally ossification of the epiphysis proceeds as did the formation of endochondral bone in the diaphysis; but the quantity of endochondral bone is here much greater, and the process of much longer duration, while the stage of provisional calcification of the cartilage is much abbreviated. The epiphysis so formed consists at first altogether of endochondral bone and is bounded towards the older bone of the diaphysis by a disc of hyaline cartilage, the epiphyseal line (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. I). The epiphyseal line is essentially responsible for the growth in length of the skeletal elements and for this purpose endures for a long time. But its growth finally comes to an end; it becomes calcified and is replaced by bone. Thus the two parts of the bone, epiphysis and diaphysis, now become united; although they differed in the location, and still more in the time of their formation.

In the ossification of the epiphysis the replacement of the cartilage never reaches the surface; there remains a layer of hyaline cartilage more or less thick, which forms the articular cartilage. Since the replacement of the embryonic cartilage by bone has been progressing unevenly, the boundary between articular cartilage and bone is never an even line, but the two substances usually interlock by means of numerous serrations.

The second post-embryonic process, which is to be seen in the bony skeleton during the early years of life, is the replacement of embryonic reticulated bone by lamellar bone. The skeleton of the adult finally contains (apart from exceptions noted above) only lamellar bone which has supplanted not merely the perichondral (periosteal) bone, but also all that which was formed endochondrally; and finally even that of the epiphysis, which, although appearing later than that of the diaphysis, has had a much greater stability. This replacement by lamellar tissue proceeds in part from the inner surface of the bone next to the marrow cavity; and in part from many small, discrete centers on the inner surface of the Haversian canals whose walls quite soon consist of lamellar tissue. Thus the remains of the reticulated bone become pressed back into the intervals between the developing lamellae of the Haversian systems. However the process of the replacement of reticulated bone does not halt here, although its advance is slow and very gradual. The remains just mentioned Pl. 10, Fig. 3 become resorbed and replaced extensively by newly-formed lamellar bone. As a Pl. 20, Fig. 1 rule the newly-formed lamellae may easily be distinguished from those which are older by the fact that they stain more intensely with the dyes commonly in use.

Naturally there takes place after birth not merely a replacement of reticulated bone by that which is lamellar but also a progressive thickening of the growing bone on its external surface through the apposition of young periosteal bone. The latter shows a lamellar structure from the first and contains, especially in its early stages, an abundance of the fibers of Sharpey.

Joints and the Connections of Bones

Cartilaginous connections of bones or synchondroses are very rare in the adult human body, but were more common during the growth of the skeleton. The hyaline cartilage which forms the union is invariably a remnant of the cartilaginous embryonic skeleton.

In ligamentous connections or syndesmoses the tissue which connects the two parts of the skeleton consists of collagenous fibrous tissue with or without elastic tissue, and occasionally of elastic tissue alone. The union of bones in syndesmoses is brought about Pl. 20, Fig. 5 essentially by the fibers of Sharpey which penetrate both the neighboring bones; this is markedly the case with the sutures of the bones of the skull.

In the human body, mixed synarthroses or symphyses are very common, occurring in the form of the intervertebral fibrocartilages. Here the external annulus fibrosus consists of rings of fibrous connective tissue with a greater or less intermixture of tiny nests of cartilage (so-called fibrocartilage — see p. 77). In general the cartilage nests are rare in the external layers of the fibrous ring, but steadily increase in number towards the central gelatinous nucleus. This gelatinous nucleus of the intervertebral discs contains the remains of the notochord in the form of vacuolated cells, which frequently show appearances of disintegration. At the same time the nucleus pulposus also contains cartilage nests. As regards the microscopic anatomy of the JOINTS proper, the articular cartilage has already been noted. The deeper layers of this cartilage display cells of irregular, or even of branched form; while its superficial layer is quite typical hyaline cartilage. In some joints, particularly those of the jaws, the surfaces of the joints are covered with fibrocartilage (not hyaline cartilage). The capsule of a joint consists, in its outer fibrous layer, of fibrillar connective tissue with a few elastic fibers; while the inner synovial layer is of connective tissue, rich in cells but relatively poor in fibers, elastic fibers being altogether lacking. Its inner surface, turned towards the cavity of the joint, is covered by a layer of endothelium which, however, is not continuous throughout. The synovial villi (fringes) have a similar structure.

Occasionally adipose tissue is found in them, and also in the deeper layers of the stratum synoviale. In this situation are also to be found blood and lymph vessels as well as sensory nerve endings.

Menisci, disci interarticulares, labra glenoidalia, and related structures consist in part of fibrocartilage and in part of dense fibrous connective tissue with but few cells and no admixture of cartilage.

II. Organs of the Blood Vascular System and of the Lymphatic System

To the organs of the vascular systems of the blood and lymph there belong, in the human body, a series of structures which have this in common; that they are composed of varieties of connective tissue and to some extent of smooth muscle, but no epithelial tissue enters into their formation. Here belong the heart (in which by exception the muscle is striated — see p. 107), the blood vessels, the lymphatic vessels, the lymph glands and smaller lymphatic structures, such as the tonsils and solitary follicles, also the spleen and perhaps the thymus.

IIa. The Blood Vascular System

The blood vessels represent a system of tubular channels which branch abundantly, the diameter varying with the grade of branching, being greatest in the large trunk vessels (arteries) in which the blood flows away from the heart, and very small in the terminal branches, the capillaries, from which there is a gradual increase towards the heart (veins). On the whole the strength of the wall undergoes similar changes, being greatest in the heart and diminishing towards the capillaries. The blood vessels which bear the blood stream from the heart to the capillaries (centrifugally) are known as arteries, *arteriae*; those which bring back the blood from the capillaries to the heart, that is to say in which the blood flows in a centripetal direction, are termed veins, *venae* (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III).

In all portions of the blood vascular system, there is a common inner lining consisting of a layer of flat cells. In contrast to the epithelium of the body this layer is termed the ENDOTHELIUM (p. 93). The endothelium is invariably a single layer of flat cells arranged in epithelial fashion and thus resembling a simple squamous epithelium. However, it is of connective-tissue origin, *i. e* it is derived from cells of the embryonic mesenchyme, and even in later life shows indications of close relationship to certain cellular elements of connective tissue, the so-called reticulo-endothelium (p. 96). Endothelial cells usually have serrated edges and are always very flat; although in large vessels (veins) which are greatly collapsed they often show considerable thickness and may appear to be in layers. The cell boundaries, like those of epithelial cells, may be demonstrated by solution of silver nitrate.

While the most delicate portions of the blood vascular system, the capillaries, consist essentially of endothelial tubes alone, there occurs in arteries and veins almost without exception an additional wall of connective tissue and muscle; in the heart the muscular wall is particularly well developed.

1. The Heart, *cor*

Pl. 23, Fig. 6

Not only by its mode of development but also in consideration of its finer structure, the heart merely represents an expanded portion of the blood vascular system, whose center it is. In two points only does it depart from the structure of the remaining portions of the blood vascular system; first through its peculiar variety of musculature (striated, see p. 107); second, because it lies in a special portion of the body cavity, the serous lining of which, as a visceral layer, covers the surface of the heart and is known as the epicardium (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II). Consequently three coats may be distinguished in the wall of the heart: 1. the inner coat, the *endocardium*; 2. the middle or muscular coat, the *myocardium*; 3. the outer coat, the *epicardium*.

Pl. 23, Fig. 6

The **endocardium** is a connective-tissue membrane of varying thickness, which covers the entire inner surface of the heart and lines the four cavities. It is much thicker in the atria than it is in the ventricles. It consists of fibrillar connective tissue with an abundance of elastic fibers which are more numerous in the endocardium of the atria where, particularly in the deeper layers, they form dense networks. In a few places, the endocardium also contains strands of smooth muscle which are especially strong in the regions of the interventricular and interatrial septa and on the atrial side of the atrioventricular valves. The endocardial surface, which is turned towards the cavity of the heart, is covered with endothelium. The elastic fibers in the thicker, atrial portions of the endocardium are not only more abundant but are also stouter than those in the thinner endocardium of the ventricles. The semilunar valves of the heart are essentially reduplicatures of the endocardium, and are devoid of vessels; while smooth muscle is present in the atrio-ventricular valves (see above). In its entire structure, the endocardium resembles the inner coat of the blood vessels (see below).

Pl. 23, Fig. 6

The **myocardium** consists of a dense network of the variety of striated muscle characteristic of the heart (p. 107); strands of this muscle are demonstrable macroscopically (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II). The individual "muscle fibers" (p. 109) are separated by a small amount of fibrillar connective tissue which, as in the skeletal muscles (p. 158) is termed the PERIMYSIUM and carries the blood vessels and nerves. In adults it contains a variable number of elastic fibers although in the ventricles little or no elastic tissue is to be found. In places the muscle passes over into tendons (*chordae tendineae*), which also contain elastic fibers but essentially represent structures of the endocardium. The *annuli fibrosi* (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II) which must be considered as the chief areas of origin of the cardiac muscle, are formed of tendinous tissue containing abundant elastic fibers.

The **epicardium** is a rather thin coat of connective tissue which contains elastic fibers. Its external surface (that is to say, the entire external surface of the heart) is covered by a simple squamous epithelium, the epithelium of the serous pericardial cavity. In the subserous tissue between epicardium and myocardium adipose tissue is often found, especially as age increases.

The heart contains an abundance of blood and lymphatic vessels and of nerves; however these are very unequally distributed to the different portions of the heart wall. The endocardium is poor in blood vessels which are present only in its deeper layers; and are entirely absent in certain situations such as the semilunar valves, and the free borders of the atrio-ventricular valves, both of which consist practically of endocardium alone. On the other hand, the myocardium is very rich in blood vessels which, in the perimysium, form dense capillary networks. The arteries of the heart are not terminal arteries, as was long considered to be the case (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II), but anastomose rather freely with one another. The epicardium contains fewer blood vessels than the myocardium but more than does the endocardium. The nerves of the heart contain fibers from the vagus nerve and many non-medullated fibers which they derive from the sympathetic nervous system. These are the motor nerves of the heart; within the heart muscle they are distinguished by forming plexuses which contain numerous nerve cells, the axones of which, as motor fibers, terminate upon the fibers of the cardiac muscle. Sensory terminations are chiefly to be found in the endocardium and epicardium. Concerning the manner of termination of the motor nerves see p. 178.

2. The Blood Vessels Proper, *vasa sanguinea*

Blood vessels are subdivided into three groups partly on the basis of their diameter and partly on that of their structure and of the direction of the blood stream within them. These groups are: 1. arteries, *arteriae*; 2. veins, *venae*; 3. capillaries, *vasa capillaria*. The endothelial tube is common to them all and is also to be found within the heart and the lymphatic vessels immediately connected with the blood vascular system; although in certain capillary areas it shows peculiarities in its structure. Consequently it has been proposed to name the endothelial coat of all blood vessels the tunica interna. As a result the capillaries would consist essentially of a tunica interna alone; while in arteries and veins there are in addition middle and external coats. However, as a rule an older subdivision is followed, and the term *tunica interna (intima) vasorum* (arteriarum et venarum) is applied to those layers of the walls of blood vessels which lie on the inner side of a layer of smooth muscle. This muscular layer may be more or less well developed, and is not always entire. In relation to the muscle of the heart the tunica interna would correspond to the endocardium. In addition there is distinguished in the vessels a middle coat, the *tunica media*, known also as the tunica muscularis because in the arteries it contains the musculature. There is also an external coat, the *tunica externa* (adventitia).

Pl. 8, Fig. 7

a. The Arteries, *arteriae*

Two varieties of tissue form the main part of the walls of arteries, elastic tissue, and smooth muscle; collagenous connective tissue and reticulum fibers are present in much smaller quantity. In the larger arterial trunks the elastic tissue predominates, not so much as fibers as in the form of numerous elastic membranes (p. 60); while in the smaller arteries this tissue decreases and muscular tissue gradually becomes more and more prominent. Thus arteries may be subdivided according to the structure of their wall, into four groups which, with certain exceptions,[1] correspond at the same time to different calibers so that the diameter of an artery may be taken as indicating its classification. There are thus distinguished: 1. very small, or precapillary arteries; 2. small arteries; 3. medium arteries; 4. large arteries. There is common to all arteries a subdivision of the wall into the three coats mentioned above, which in most arteries are sharply marked off from one another.

Pl. 23, Figs. 1—4

Pl. 24, Figs. 2, 3, 5, 6

Pl. 23, Fig. 4

The very small or PRECAPILLARY ARTERIES (ARTERIOLES) show a very simply formed intima, that is to say it consists only of endothelium and a wavy, corrugated elastic membrane, the lamina elastica interna, which is a fenestrated membrane (p. 60) and is present

Pl. 24, Fig. 6

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[1] Such exceptions are regional differences, *i. e.* differences in the structure of the walls of arteries of the same diameter but of different regions of the body; however such differences are less frequent than is the case with the walls of veins.

in all arteries. Upon this membrane rests the bare endothelium in the form of elongated, almost spindle-shaped cells whose long axis is parallel to that of the vessel. The media of precapillary arteries consists of a very few (one, two, or three) layers of smooth muscle fibers which are small in size, and whose nuclei alternate if in more than one layer. Between the muscle fibers is found a very small number of delicate elastic fibers. The externa (adventitia) is formed of bundles of connective tissue and fine elastic fibers, both of which run longitudinally. As is the case with all blood vessels, the adventitia passes without sharp Pl. 23, Fig. 4 demarcation into the surrounding connective tissue. Elastic elements in this class of arteries Pl. 24, Fig. 5 are thus almost confined to the intima and adventitia.

The SMALL ARTERIES (about the size of a digital artery) show as regards the finer structure of the intima the same characteristics as are found in the precapillary arteries. On the other hand the media of small arteries consists of a large number of layers of smooth muscle between which a number of fine elastic fibers run circularly. Thus, although the muscle greatly predominates, it is no longer the only constituent of the media. The externa shows a structure similar to that of the arterioles; however there are greater numbers of elastic fibers, dense groups of which run longitudinal courses near the media and form a more or less sharp boundary layer known as the elastic coat of the adventitia (tunica elastica externa). This elastica externa is often very prominent in quite small arteries but is less marked than the elastica interna and does not, like the latter, consist of a simple membrane. In many arteries it is indistinct or entirely lacking, *e. g.* in the arteries of the brain, and those of the fingers; the latter, however, have particularly strong muscular coats.

The ARTERIES OF MEDIUM SIZE include most of those arteries of the body which have Pl. 23, Figs. 1, 2 received special names; notable exceptions are the aorta and pulmonary arteries, their Pl. 24, Figs. 2, 3 direct branches, and a few other arteries, *e. g.* the vertebral artery. Arteries of medium size are distinguished from smaller arteries by containing in the intima, in addition to the endothelium and elastica interna, fine longitudinal connective-tissue bundles which contain nuclei, but whose collagenous nature is doubtful. Many longitudinal elastic fibers are also present in the intima which is decidedly thicker than it is in arteries of less caliber. The middle coat of these arteries of medium size shows a distinct increase in the amount of elastic tissue which takes the form not only of stout fibers and networks of fibers running in a circular direction, but also in part of delicate elastic fenestrated membranes (p. 60). In addition to the circular fibers in the outer layers of the media there are present radial or arcuate elastic fibers. The elastic membranes lie between the different layers of the circular muscle, surrounded by fine strands of fibrillar connective tissue; as a rule their size and numbers increase as the diameter of the artery enlarges and its walls grow thicker. The externa of arteries of medium size contains strong elastic fibers in abundance, which like those of smaller arteries run longitudinally. Vasa vasorum (see below) are also present. These three groups of arteries belong to the muscular structural type, *i. e.* the muscle predominates over the elastic tissue.

Pl. 23, Fig. 3 The LARGE ARTERIES are of predominantly elastic type and comprise, as previously mentioned, the pulmonary artery, the aorta, and their immediate branches.[1] On the whole, the intima shows the same structure as in arteries of medium size; however, it is even thicker, its elastic elements increase in density towards the media and smooth muscle is occasionally present. The endothelial cells are shorter and more polygonal, while collagenous tissue is clearly seen among the elastic fibers. A true elastica interna is lacking; in its place there is a network of stout elastic fibers. The media of the larger arteries is uncommonly rich in elastic tissue, the yellow color of which, is noticeable even macroscopically. The muscular tissue is greatly diminished but does not wholly disappear; although for a short distance at their origins the aorta and the pulmonary artery contain practically no muscle. The elastic tissue, which now predominates so greatly, appears chiefly in the form of numerous (about 40–50) concentric elastic membranes, more rarely in the form of coarse fibers. In the intervals between the elastic membranes, some of which are fenestrated while others are unbroken, there are found connecting elastic fibers which naturally form networks. In addition, in the same situations there are present relatively slender bundles of smooth muscle fibers which are short and often branched. Usually, but not invariably, their course is strictly circular. An elastica externa is lacking in the larger arteries. The adventitia shows about the same structure as in vessels of medium size; however, in places smooth muscle fibers appear and longitudinal muscle is constantly present in the aortic adventitia of most mammals. Naturally the external coat contains the vasa vasorum.

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[1] The features of the larger arterial trunks are not everywhere the same. While the common carotid arteries as far as their bifurcation, the subclavian and axillary arteries and the common iliac arteries show the same structure as the wall of the aorta, others, such as the coeliac artery and the external iliac and femoral arteries, incline more to the structure of arteries of medium size in spite of their relatively large diameter. There are also certain regional differences in the structure of the individual larger arteries. On the other hand, the vertebral artery has the same structure as have the great branches of the aorta.

Pl. 23, Fig. 3

PECULIARITIES of structure are rare in arteries, and when they do occur are largely regional. In veins, the condition is just the opposite. The arteries of the brain and of the cranial cavity in general, have indeed a very stout and distinct elastic interna; but otherwise they are very poor in elastic tissue, both in the media and in the externa. Many arteries of small or medium diameter show occasionally in the adventitia a few scattered bundles of longitudinal smooth muscle, actually the only muscular elements to be observed in the externa of human arteries. The arteries of the chorioidea of the eye are almost entirely devoid of muscle and have only a few peculiarly arranged muscle fibers. In rare cases, chiefly in the umbilical arteries, strands of longitudinal muscle lie within the media.[1]

The walls of arteries contain blood vessels, *vasa vasorum*, for purposes of nourishment. Almost without exception they are confined to the adventitia and to the most external layers of the media. Nerves, both of medullated and of non-medullated fibers, are found in all three layers of the arterial wall. The sensory (?) fibers form networks within the intima and adventitia, while the motor fibers supply the media; however the vessels of the substance of the brain possess no nerves.

Pl. 23, Figs. 2, 3

b. The Veins, *venae*

Veins differ from arteries in the structure of their walls chiefly in containing a much smaller quantity of muscle, which occasionally is altogether lacking, also through a much diminished content of elastic tissue with a corresponding increase in the amount of collagenous tissue. Veins are more difficult to classify than are the arteries; a subdivision into veins containing much muscle, those containing little muscle and those entirely free from muscle, might be made; but the strength and thickness of the wall do not depend on diameter alone but on other circumstances, such as the position of the vessel (whether in an extremity, the skin, abdominal, organ, or cranium). Many veins, such as those of the

Pl. 24, Figs. 1, 3, 4

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[1] Concerning the sheathed arteries of the spleen and the buds of Schmidt in the thyreoid arteries see the descriptions of the organs in question.

abdomen and cranium, contain extremely little muscle; the veins of the bones (Brechet's veins), of the meninges and of the brain itself, of the retina and chorioid coat of the eyeball and those in the trabeculae of the spleen are entirely devoid of muscle. On the contrary many veins of the skin contain large quantities of muscle so that their walls are scarcely weaker than those of arteries of the same diameter; while elsewhere veins have much thinner walls than have the arteries which they accompany. Small postcapillary veins are often like the capillaries themselves in structure; they contain no muscle and are as yet free from elastic tissue.

The muscle of veins is divided between the media and the adventitia and never has the compact character which it has in arteries, nor is it always circular in direction but frequently is arranged longitudinally. Indeed in many veins smooth muscle occurs within the intima itself (see below). Consequently veins of similar diameter may show very dissimilar structure and great difference in the thickness of their walls. Regional relations greatly affect the structure of veins; those of the lower extremities invariably containing more muscle than do those of the upper parts of the body, particularly than those of the head and neck.

As a rule the veins contain much less elastic material than do the arteries. A true elastica interna is never present, and as a result delimitation of the layers of the vessel wall is difficult. Even in veins in which muscle is prominent the media contains comparatively little; and in some veins it is scarcely demonstrable in the media. On the other hand the adventitia of many veins, unlike that of the arteries, contains large quantities of muscle. The large trunk veins which empty into the heart always have striated fibers of cardiac muscle within their walls for a short distance. In addition, in many veins there are also inner strands of longitudinal muscle. Thus it is not merely in the amount, but also in the distribution of the muscle that the walls of veins differ so markedly from those of arteries.

Pl. 24, Figs. 1, 3. 4

In veins, the INTIMA is rarely well developed. In addition to the endothelium it contains collagenous connective tissue, but only a few elastic fibers. In many veins it is reduced to a minimum, and even many of the larger veins (vena cava superior, jugular, and axillary veins, portal vein and others) have only an endothelium to represent the intima; so that smaller veins frequently have a thicker intima than do the larger. The endothelial cells of veins are less elongated and more polygonal than are those of arteries. The VALVES of the veins are reduplications of the intima, in which the elastic tissue lies chiefly on the side towards the blood stream, on which side also the endothelial cells usually lie longitudinally; while on the opposite side their long axes are transverse. Towards the media the elastic elements of the intima of veins do not combine to form a true elastica interna; but for the most part, though not invariably, they form a dense fibrous network at the boundary between intima and media. On the other hand, in the intima of many veins there is found smooth muscle which commonly, as in the femoral and popliteal veins, runs longitudinally. Muscle is exceptionally abundant for some distance in the wall of the dorsal vein of the penis where it has special functional significance.

The MEDIA of veins, as far as it exists at all, shows the same elements as does that of arteries; that is to say, it consists of circular muscle and networks of elastic fibers. But it also invariably contains a large quantity of collagenous connective tissue, so that the musculature appears much less compact than it does in arteries; even in veins which have quite thick middle coats the bundles of muscle are scattered in connective tissue. But commonly the media of veins is either very much reduced or is altogether lacking (as in the veins of the skull and of the bones, retinal and chorioid veins, the vena cava superior,

Pl. 24. Fig. 1

and all postcapillary veins); that is to say, in place of the muscle there is present a small quantity of fibrillar connective tissue. In such cases the layer as a whole is very thin.

Pl. 24. Fig. 5

The EXTERNA (ADVENTITIA) as a rule is the most strongly developed coat in the walls of veins. In contrast to its condition in arteries it is never sharply marked off from the media; in particular an elastica externa is usually wanting, although occasionally elastic fibers are grouped into a compact limiting membrane. In addition to fibrillar connective tissue and a few longitudinal elastic fibers there occur in the adventitia of many veins fibers of longitudinal muscle which may even become assembled to form a very a thick layer, as in the renal and suprarenal veins and the portal vein. The degree of development of longitudinal muscle in veins is thus highly variable. For instance in the extremities there are veins with well developed media but no longitudinal muscle in the adventitia; on the other hand there are abdominal veins (suprarenal veins) with quite weak media and a heavy longitudinal musculature in the adventitia. The thickness of the adventitia varies to a corresponding degree. Longitudinal muscle often is most abundant in veins with weak media; so that taking the latter together with the weak intima, almost the entire thickness of the wall is due to the externa and its large content of muscle.

Blood vessels and nerves have the same relations in veins as they have in arteries.

c. The Capillaries, *vasa capillaria*

Pl. 23. Fig. 5
Pl. 8. Fig. 8

The capillaries are a system of extremely narrow and entirely microscopic vessels interposed between arteries and veins. On the one side the finest precapillary arterial branches, having lost all their muscle, pass into the arterial capillaries. On the other side the smallest branches of the veins, which as yet have no media (p. 146) and are surrounded merely by a connective-tissue adventitia, are formed from the venous capillaries. The essentials of a capillary are: first, that its wall consist of a simple endothelial tube; second, that it contain no muscular elements; third, that in contrast to arteries and veins, which in branching always become smaller, the branching of capillaries does not result in change of diameter. However, the diameter of capillaries does vary in different tissues and organs. There are wide capillaries (lungs, liver, marrow etc., 12—15 μ and more, even up to 50 μ) and narrow capillaries (muscles, retina, 6—8 μ). The wide capillaries usually form networks with small meshes and the narrow capillaries networks with large meshes.

At the points of transition of arteries into capillaries and of capillaries into veins the diameter of the vessels usually is decidedly greater (up to 50 μ) than in the true capillary area itself. Certain connective tissue cells (histiocytes) of the adventitia commonly assume the form of stellate cells and are applied in large numbers to the beginnings of the capillaries, thus forming a kind of "adventitia capillaris". These have been termed ROUGET cells after their discoverer. That they are responsible for the contractility of the capillaries, or that they are continuous with the smooth muscle cells of arteries or veins, has by no means been demonstrated. Moreover in many places, *e. g.* the skin, it may be shown that the capillaries consist of only a simple endothelial tube, the so-called ROUGET cells being here entirely absent. Without doubt Rouget cells, where they occur, are ordinary histiocytes, not contractile elements.[1]

In addition to the simple tube of endothelium capillaries possess a delicate basal membrane composed of a network of precollagenous reticulum fibers. This network is Pl. 8, Fig. 8 easily demonstrated by silver-impregnation and other methods. Similar fibrous elements share in forming the wall of the venous capillaries in the splenic pulp (see the chapter on the spleen).

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[1] Nevertheless fresh evidence is from time to time being brought forward in support of the contractile function of the Rouget cells. — Trans. note.

The endothelial cells which form the capillary wall are trough-shaped because of the small diameter of the vessels. They are elongated, and lie with their long axes parallel to that of the vessel. As a rule, like the endothelium of arteries and veins, their cell boundaries may be demonstrated by solution of silver nitrate which blackens the cement between the flat cells. The breadth of the cells is often but slight, although in places there are local expansions. In a few regions, as in the capillaries of the liver, the looped capillaries of the renal glomerulus and the capillaries of the choriocapillaris of the chorioid coat of the eye, it is not possible to demonstrate cell boundaries; consequently it has been assumed that in these situations the capillary tube is formed of a nucleated syncytium.

Fine non-medullated nerve fibers surround the capillaries, but do not accompany them throughout their entire length. The nuclei of SCHWANN lie close to the capillary wall, apparently often fastened to it. The nerve fibers often loop around the capillaries and after dividing dichotomously terminate on the endothelial wall in delicate, free end-bulbs.

In all higher vertebrates blood vessels are developed from the middle germ layer, or more precisely from the mesenchyme. Embryonic mesenchyme, or connective-tissue cells, become grouped together in connected series and surround a lumen which later is that of a main trunk vessel, *e. g.* the aorta. The development of branches then follows similarly to the formation of vessels in later life; that is to say, solid cellular outgrowths are formed from the vessel wall, which later become excavated.

IIb. The Lymphatic System

To the lymphatic system there belong, in the first place, the lymphatic vessels and the lymph, next the lymph glands interposed along the course of the lymph stream and smaller lymphatic structures, the lymph nodules. Standing in very close relation to the lymphatic system is the spleen and possibly the thymus.

1. The Lymphatic Vessels

Since the lymphatic vessels are only a subordinate extension of the blood vessels, especially of the veins into which they discharge, they differ in structure but little from the latter. The chief difference is that there exists but one type of lymphatic capillary and vessel. The contrast which exists between arteries and veins does not occur here, because the lymph stream flows in the same direction (centripetally) in all lymphatic vessels. The lymphatic capillaries and vessels of lesser diameter are, like the blood capillaries, mere Pl. 53, Fig. 2 endothelial tubes. But they have much less regular walls and a more variable diameter than do the corresponding blood capillaries. In their walls there may be demonstrated precollagenous reticulum fibers upon which the endothelium rests. The only difference between lymphatic capillaries and the smaller non-capillary lymphatic vessels is that the latter have numerous valves, while the former have none. On the other hand, the medium and larger lymphatic vessels show a structure similar to that of veins in possessing a layer of circularly arranged smooth muscle and in the main stems a longitudinal layer as well. The relations to elastic tissue are similar to those of the blood vessels. Thus there may be distinguished, at least in the larger main vessels, a weak intima with longitudinal elastic fibers; a media with circular smooth muscle and some elastic fibers and an adventitia with longitudinal elastic fibers and muscular elements. It is probable that with the exception of certain organs, *e. g.* the eyeball, the lymphatic vessels everywhere begin, not with open tissue spaces, but with closed pathways, the lymphatic capillaries. Nor is it very probable that the serous cavities of the body communicate with the lymphatic radicles through preformed openings, although the contrary is frequently assumed and a name, stomata, given to the supposed openings. Neither do actual openings in the walls of the capillary blood vessels occur; perhaps with the exception of the splenic sinuses in which such stomata have recently been described. Leucocytes penetrate the walls of both blood and lymphatic vessels by using temporary openings made through the cement between the endothelial cells. These openings close again after the leucocytes have passed through.

2. The Lymph Glands, *lymphoglandulae*

The lymph glands, or better the lymph nodes, are bodies of widely varying sizes, which consist of adenoid tissue (p. 72) and bear only superficial resemblance to glands. They are interposed like filters along the path of the lymph and are usually kidney- or bean-shaped with the vessels which bring the lymph, the *vasa afferentia*, entering the convex side. The vessels which carry away the lymph, the *vasa efferentia*, are usually fewer in number and leave from the concave side of the organ through a depression termed the hilum, which also serves for the entrance and exit of the blood vessels.

Pl. 25, Figs 1, 2
Fig. 16

The lymph glands are surrounded by a connective tissue capsule which regularly contains elastic fibers and smooth muscle, the latter being especially abundant in the lymph nodes of many animals, *e. g.* cattle. The capsule sends processes, erroneously termed TRABECULAE, into the interior of the gland. In reality they are septa which in section simulate trabeculae. They give off lateral branches which anastomose, consequently the trabeculae form a connective tissue framework for the lymph gland. In man this framework, like the trabeculae or rather septa of which it is composed, is not nearly so well developed as it is in the lymph glands of many animals, *e. g.* cattle. The substance of the lymph gland consists of reticular connective tissue attached to the trabecular network; the reticulum represents the stroma of the lymph gland while the parenchyma is represented by the closely packed lymph cells (p. 72). The latter are so disposed that a medulla formed of cords can be distinguished from a cortex composed of rounded or pear-shaped bodies.

The **cortex** of the lymph glands is chiefly disposed around the convexity of the gland, and presents a number of rounded bodies, the lymph knots or follicles, or SECONDARY NODULES, also called cortical nodules, which are separated by the trabeculae. Their number varies according to the size of the organ and occasionally neighboring follicles are fused together. These SECONDARY NODULES of the lymph glands consists of lymph cells which are placed close together at the periphery of the nodule; while at its centre there is a clear zone, the GERMINAL CENTRE. In the latter the lymph cells are somewhat larger and show distinctly the figures of mitotic division, hence the term lymphoblasts applied to them. Around the germinal center the lymph cells stand closer together, often in regular rows. The reticulum of the knots is extremely fine and delicate, and usually is only to be demonstrated by shaking the lymph cells out of the section. It consists of reticular tissue (p. 72) in which fine precollagenous fibers are demonstrable.

Pl. 25, Fig. 1
Pl. 25, Fig. 2
Pl. 1, Figs. 4, 5
Fig. 16

The **medulla** of the lymph glands is composed of thick, irregular, anastomosing strands of parenchyma, the MEDULLARY CORDS. These like the cortical follicles consist of adenoid tissue; they proceed from the cortex where they connect with the follicles, and

Pl. 25, Fig. 1
Fig. 16

extend through the whole medulla, anastomosing with one another. They are distinguished from the nodules of the cortex only by the lack of germ centers; although in general the massing of the leucocytes is a little less dense and the reticulum a little more stoutly formed, than in the cortex. Between the medullary cords and the periphery of the secondary nodules on the one hand, and the trabeculae on the other, there lie spaces which together form the lymph sinus and which represent enlarged lymphatic vessels interposed in the path of the lymph. The sinuses are wide, very irregular lymphatic spaces, lined by the endothelium of the lymphatic wall and are more or less completely filled by free-moving lymphocytes.[1]

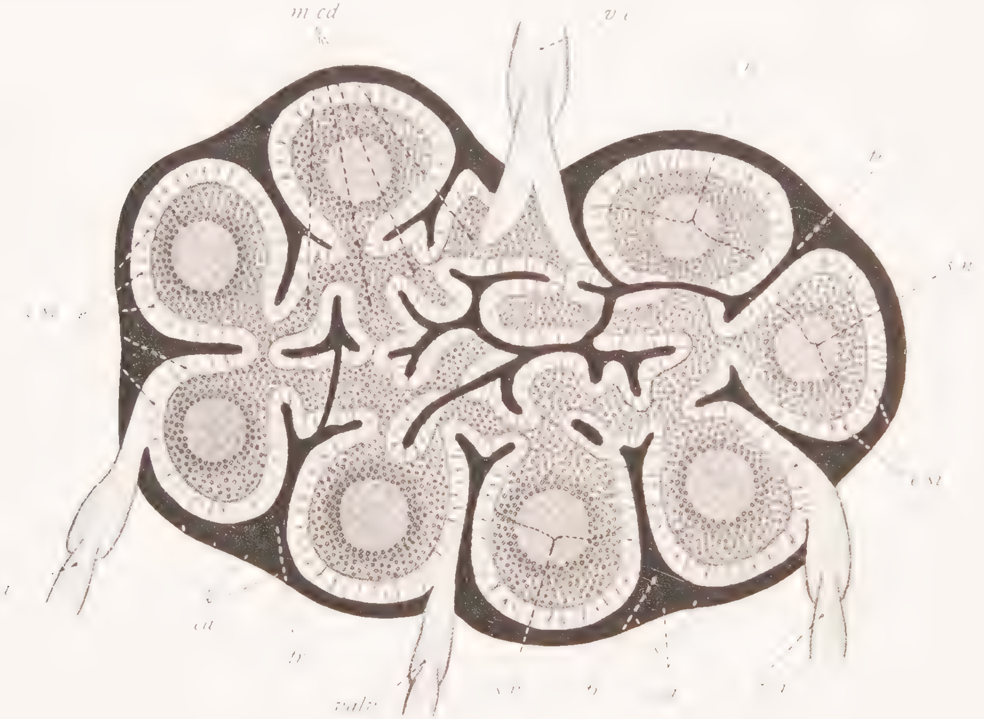

Fig. 16. **Diagram of the Structure of a Lymph Gland**

Clear: lumen of lymphatic vessels and lymph sinus.
Dotted: adenoid tissue (germinal centers coarsely dotted but paler in tone).
Black: capsule and trabecule.

ca = capsule
c si = cortical sinus (marginal sinus)
m cd = medullary cords
s n = secondary nodules
tr = trabeculae (septa)
v a = vasa afferentia
valv = valves of the lymphatic vessels
v e = vas efferens

The connections between the capsule and septa on the one hand and the follicles on the other, are not very well developed in man; thus at times the follicles almost give the impression of floating in the marginal sinus. The afferent lymphatic vessels, which it will be recalled are in the majority, discharge at different places into the marginal sinuses separating capsule and septum from the cortical follicles; while the efferent lymphatic vessels arise from the lymph sinuses of the medulla lying between the lymphatic medullary cords. In such manner, the lymph gland is interposed like a filter in the lymph stream and the lymph traverses it along complicated pathways which run essentially from cortex to Fig. 16 medulla.

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[1] The lymph sinus and the trabecular branches crossing it are best seen in frozen sections from which the cells have been shaken out.

The endothelial lining of the lymph sinus ensheaths, so to speak, the follicles and the medullary cords as well; both of which thus appear covered by a superficial endothelial layer.

The endothelium of the lymph sinus stands in direct connection with the cells of the reticulum (reticulo-endothelium, p. 95). Both of these types of cells possess phagocytic qualities to a high degree; consequently they frequently become loaded with dustlike foreign matter which is carried along the pathway of the lymph into the lymph gland.

Beside typical lymphocytes there occasionally are present in the lymph gland modified types of leucocytes, such as eosinophiles, plasma cells and mast cells.

The lymph glands are rich in BLOOD VESSELS; the arteries usually enter at the hilum at which spot the veins leave the gland. At the hilum the connective-tissue trabeculae converge and surround the blood and lymphatic vessels as they pass either inward or outward; there is thus formed, as it were, a connective tissue sheath for the vessels. The larger arterial branches usually run in the trabeculae, while the smaller enter into the secondary nodules. The nerves of the lymph gland are essentially of the sympathetic system and for the most part accompany the blood vessels.

3. The Lymph Nodules, *noduli lymphatici*

Lymph nodules may appear either singly *(noduli lymphatici solitarii)* or in groups Pl. 48, Fig. 1 *(noduli lymphatici aggregati)* as in the tonsils and in Peyer's patches. In structure they Pl. 49, Fig. 3 resemble the secondary nodules of the lymph glands but have no lymph sinus and are Pl. 50, Figs. 2, 4 also devoid of any special connective tissue covering or capsule. Thus they stand in only Pl. 53, Fig. 1 a very loose connection with the system of lymphatic vessels; in particular they are not interposed in the path of the lymph as are the true lymph glands; moreover they have only efferent lymphatic vessels. They are composed of rounded, more or less connected accumulations of leucocytes, with a distinct germinal center in the interior of each individual mass of lymphatic cells. They are, for the most part, situated in the mucous coat of many abdominal organs, *e. g.* the digestive tract (see the organs in question).

It is very probable that the smaller of these structures are not permanent, but may be newly formed in any suitable locality and then again may disappear. Consequently there are seen all transitions from the diffuse lymphatic tissue of many mucous membranes, through a distinctly circumscribed accumulation of lymph cells, to the fully developed lymphatic nodule with germinal center.

4. The Spleen, *lien*

The spleen has in general a structure somewhat similar to that of a lymph gland, in particular it consists of adenoid (lymphatic) tissue and is thus not a true gland. However Pl. 25, Figs. 3–5 it differs from a lymph gland in having relations to the blood stream which are similar Pl. 26, Figs. 1, 2 to the relations of lymph glands to the lymph. Thus in the lymph gland there are lymph Fig. 17 sinuses and in the spleen blood sinuses which contain blood, not lymph. On the other hand lymphatic vessels are entirely lacking in the spleen. Furthermore, the disposition of the splenic corpuscles, which are homologous with the secondary nodules of the lymph glands, is bound up with the disposition of the blood vessels (arteries) and in other ways as well the structure of the spleen differs in details from that of the lymph glands.

The spleen is surrounded by a CONNECTIVE-TISSUE **capsule,** the *tunica albuginea*, which is much stouter than the corresponding capsule of a lymph gland. The splenic capsule, especially in its deeper layers, is rich in elastic fibers; but in man it is poor in muscle fibers although in many animals it always contains smooth muscle in large amount. It is fused with the peritoneal membrane covering the spleen, and consequently shows on its surface the serous peritoneal epithelium; only in the region of the hilum is the fusion somewhat less intimate. The capsule sends very strong cordlike processes similar in structure to itself, the splenic trabeculae, *trabeculae lienis*, into the interior of the spleen where they act similarly to those of a lymph gland; *i. e.* after many branchings and anastomoses they finally pass into the reticulum. There is no question here of septa; these are true trabeculae. The reticular connective tissue is extremely tender within the splenic corpuscle but is coarser in the splenic pulp. At the same time the trabeculae carry the large branches of the blood vessels, especially the veins. Beside many elastic fibers they also contain, even in man, some smooth muscle, indeed more than does the capsule. The trabeculae are distinctly thicker than the capsule; often they attain this increased thickness only at some distance from the surface by anastomosing with neighboring trabeculae. Usually they have a flattened cylindrical form.

The PARENCHYMA OF THE SPLEEN fills the meshes of the trabecular network, but does not, as in the lymph glands, show a subdivision into cortex and medulla; moreover the splenic corpuscles, which correspond to the cortical nodules, are distributed like islands throughout the entire spleen. They have been termed "grey pulp". The true splenic pulp, *pulpa lienis*, also termed "red pulp", lies between the splenic corpuscles.

The **splenic corpuscles** (of Malpighi), *noduli lymphatici lienis*, ordinarily appear in
Pl. 25. Fig. 3 sections of the spleen as rounded bodies which contain a small artery, usually in a markedly
Pl. 26. Fig. 1 eccentric position. They consist of lymph cells placed close together with a germinal center at the middle; however the germinal center is often less distinct than in the secondary nodules of the lymph gland and may be entirely lacking, especially in old age. The splenic corpuscle thus corresponds to the secondary nodule of the lymph gland, except for the artery which penetrates it; this artery (so-called central artery) is lacking in the lymph gland, at least in the typical form of the latter.

The splenic corpuscles have a diameter of 0.2—0.3 mm. In man they are commonly spherical in form, but may be short cylindrical or short fusiform structures with vaguely defined ends; in many animals, on the contrary, they are distinctly cylindrical. The corpuscle is not sharply marked off from the surrounding pulp, at least not in man, but its limits are often indicated by fine elastic fibers. The splenic corpuscle really represents a moderate enlargement of the lymphoid sheath of the smaller splenic arteries.

Before dealing with the structure of the splenic pulp, a glance must be taken at the relations of the **blood vessels** in the spleen, since these determine to a quite extraordinary degree the structure of the splenic pulp.

Unfortunately up to the present there exists no unanimity of view as to the circulation of blood in the spleen. While, upon grounds explained below, in this text the conception is followed that in the splenic pulp, as in the body in general, the circulation is closed, others hold that the blood flows through the pulp not in closed vessels but as through a sponge.

The chief arterial trunks which enter the spleen lie at first within the trabeculae and are clearly distinguished from their accompanying veins by the fact that they retain their own wall which has relatively much muscle; while the veins have no wall distinct from the substance of the trabeculae. The smaller arterial branches on leaving the trabeculae lose their trabecular fibro-elastic sheath, the place of which is gradually taken by one of lymphoid character (arterial branches of 0.2—0.15 mm. diameter). The MALPIGHIAN CORPUSCLES are thickenings of these sheaths, and lie chiefly at the points of division of the small arteries. The arteries traverse the corpuscles eccentrically, thus they never pass through a germinal center. It is evident that a section of a splenic corpuscle may pass through two or three arterial branches (so-called central arteries) instead of a single

Fig. 17

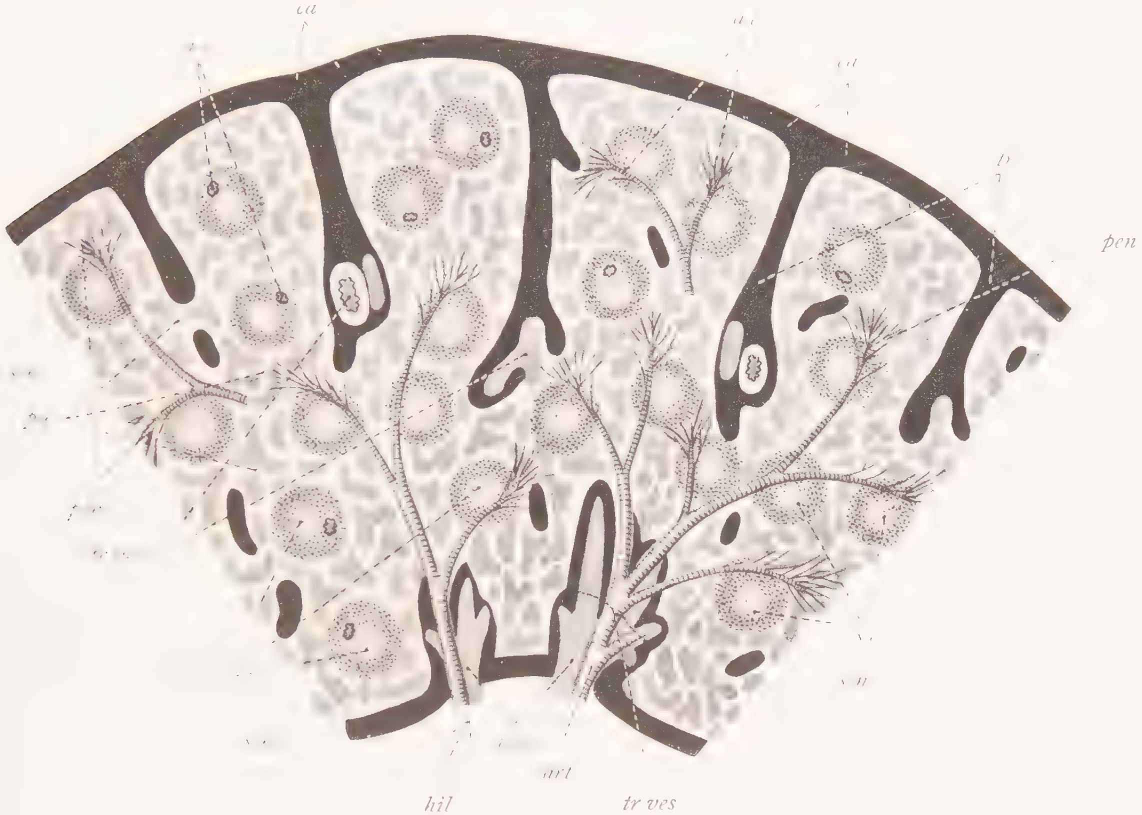

Fig. 17. **Diagram of the Structure of the Spleen**

Above is seen the convex outer surface of the spleen and at the bottom the concavity of the hilum. Capsule and trabeculae are black; arteries are marked transversely; veins, including the venous sinuses of the pulp, dark grey; pulp light grey; splenic corpuscles dotted.

a c = central arteries
art = larger arterial branches
ca = capsule
hil = hilum
pen = penicilli
pu = pulp
sin = splenic sinuses
s c = splenic corpuscles
tr = trabeculae
tr ves = trabecular vessels
ven = larger veins

one, since the corpuscles as mentioned above are situated upon the division points of the arteries.

Fig. 17 After passing through the splenic corpuscle the central arteries show a diameter of about 0.05 mm. Upon entering the pulp they at once break up into a number of precapillary arterioles, which upon maceration show a brushlike form, the so-called penicilli. These fine arterioles (about 30 μ in diameter) lie in the pulp and retain their smooth muscle but show a connective tissue thickening of their wall (so-called sheathed arteries) before they pass over into capillaries.[1]

In its passage through the splenic corpuscle the central artery not only gives off the capillaries for the nodule, but elastic fibers pass from the arterial wall into the nodular tissue. The so-called venous capillaries of the splenic pulp, which arise from the sheathed arteries, show very peculiar relations. Because of the great relative width of their lumina these pulp capillaries are also called splenic sinuses. They anastomose abundantly and extend throughout the whole region of the pulp so that the latter really represents only the material which fills in between the sinuses. The latter occupy more space than the pulp tissue and, as mentioned, are to be considered as dilated capillaries whose width varies greatly according to their state of distention.

Pl. 20, Fig. 2

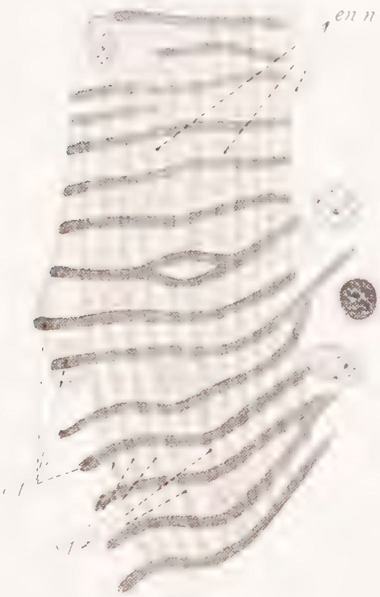

Fig. 18. **Diagram of the Structure of the Wall of a Splenic Sinus** (after MOLLIER).

The wall of the sinus is represented in a distended condition in order to display the "fenestrations".

c f = circular fibers
en n = endothelial nuclei
s f = so-called splenic fibers

Those who adhere to the view of an intermediary blood stream in the spleen hold that the walls of the splenic sinus cease after extending a certain distance, that the tissue of their wall passes into the reticulum of the pulp and that the blood then streams through the pulp and is in direct contact with its cells. The views on the structure of the sinus wall are almost equally matters of dispute. The view here given seems to possess the highest degree of probability.

Fig. 18 The sinus lacks a membrane of its own which would correspond to the basal membrane
Pl. 25, Fig. 4 of a capillary. The wall consists of only two structural elements, the so-called splenic fibers on the one hand, and the external circular fibers on the other. The former represent the innermost layer of the sinus wall; they run longitudinally, contain nuclei and thus correspond to the endothelial cells of other capillaries. However they are distinguished from ordinary endothelial cells in not being clearly defined cellular elements, but in constituting a netlike syncytium; since the longitudinal elements do not form an unbroken layer, but stand in connection with one another through anastomoses in which no cell boundaries are

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[1] The former name, still somewhat in use, of "capillary sheaths" (of Schweigger-Seidel) comes from the erroneous idea that these vessels are capillaries with thickened walls. They are much more fully developed in the spleens of many animals than in the human spleen.

demonstrable. In this peculiarity the wall of the sinus agrees with that of the capillaries of the liver and of the renal glomeruli. When the sinus is empty the part of the splenic fiber which contains the nucleus often projects distinctly beyond the wall into the sinus.

External to this syncytial association of elongated, fiberlike endothelial cells there follows the layer of circular fibers first described by HENLE, which was long held to be of elastic nature and may indeed be formed of pre-elastic fibers. The ringlike fibrous elements Fig. 18 are placed at slightly varying intervals and are connected by an abundance of oblique anastomoses. These two structural elements of the sinus wall are by no means independent of each other; on the contrary not only do the circular fibers lie close against the longitudinal fibers of the syncytium but probably the two are directly united by delicate connections of protoplasm.

Since neither the longitudinal "fibers" of the inner layer nor the circular fibers exterior to them lie in immediate contact with their neighbors of the same layer there are openings left between them, openings which naturally are larger when the sinus is filled with blood and smaller when it is empty; *i. e.* when the wall is less distended. This explains the fact that red blood cells can pass through these openings in the walls when the sinus wall is stretched, *i. e.* when the spaces are large enough; while in the undistended condition of the wall the spaces are too small for the passage of erythrocytes.

This structure of the sinus wall is also a sufficient explanation of the fact that in spite of the closed circulation within the spleen, red blood corpuscles do pass into the pulp; but their number in the latter situation is much less than in the circulating blood itself.

There are two chief objections to the opposite conception of an intermediary circulation. In the first place it is possible (Pl. 26, Fig. 2) by careful injection to fill the splenic sinuses without having the injection pass into the pulp. In the second place if the circulation were quite open the number of erythrocytes lying in the pulp would be decidedly greater than it actually is.

While the venous capillaries of the splenic pulp, the sinuses just described, are derived from the so-called arterial capillaries of both splenic corpuscles and pulp (that is from the capillary branches of the sheathed arteries), the splenic sinuses are continued into the small veins of the pulp, which like the trabecular veins are very thin-walled vessels quite devoid of muscle.

As regards the CELLULAR ELEMENTS OF THE SPLENIC PULP they are situated in the reticulum, which in man is very poorly developed. It consists primarily of most delicate extensions from the trabecular system and is typical reticular connective tissue; but it contains no elastic fibers, a point of contrast with the trabeculae in which such fibers are very numerous. The reticulum of the pulp passes without sharp demarcation into the splenic nodules on one hand, and into the tissue of the sinus wall on the other. However the delicate elastic fibers which are abundant in the splenic nodules, but as just mentioned are lacking in the pulp, may serve to form a moderately sharp boundary between the two constituents of the splenic parenchyma.

The cells of the splenic pulp which are situated in the reticular tissue have been Pl. 25, Fig. 5 termed **splenic cells** or **myelocytes.** They are mononuclear cells belonging to the great group of the lymphocytes but are decidedly larger and have more abundant protoplasm than the lymphocytes of the nodules, particularly than those of the border zone. It is these myelocytes which form the greater part of the cords of cells in the pulp and which phagocytose the red blood corpuscles after the latter have escaped from the sinus. Consequently in the tissue of the pulp some erythrocytes are always to be found intact, others only as fragments. When erythrocytes have been phagocytosed by the splenic cells there is produced a picture of cells containing blood corpuscles. In the same locality cells are to be found containing pigment derived from the phagocytosed blood corpuscles; free pigment is also present. Along with these splenic lymphocytes other forms of colorless blood cells, such as granulocytes (neutro-, oxy- and baso-philic) and plasma cells are constantly found in the splenic pulp, although to a variable extent.

The BLOOD VESSELS of the spleen have already been described. Lymphatic vessels are completely lacking in the splenic tissue proper. The spleen is one of the few organs, which, except in its capsule, contains no LYMPHATIC VESSELS. On the other hand, the spleen is rich in NERVES which are stout trunks consisting almost exclusively of non-medullated, sympathetic fibers. These accompany the vessels and probably serve primarily for the innervation of their muscle and also for that of the muscle of the trabeculae. The nerves also form fine plexuses in the pulp, which however bear no nerve cells. The splenic nerves contain a few medullated fibers but whether the latter are of sensory nature is unknown.

The splenic pulp of many mammals contains giant cells (megakaryocytes p. 93).

In many mammals (sheep, cattle) there frequently occur bodies which are very similar in structure to the spleen and which have been termed HAEMOLYMPH GLANDS; in man only indications of their presence are to be found. In the haemolymph glands red corpuscles in large number disintegrate. Frequently in the arrangements of their blood vessels etc. they correspond fully to the structure of the spleen. They often receive lymphatic vessels and then represent a structure intermediate between spleen and lymph gland. The accessory spleens which are not infrequently found in man are exactly similar in structure to the main organ.

5. The Thymus, *glandula thymus*

Because of its structure, the thymus is usually considered a lymphatic or adenoid organ; although it is developed from the epithelium of the third and fourth pharyngeal pouches and its early anlage is beyond doubt altogether epithelial. Later in development the greater part of the cells forming the "gland" have an appearance extremely like that of lymphocytes; so that the characteristic cells of the thymus, that is to say the small cells of the cortex (see below), are not to be distingiushed from true lymphocytes. Consequently it is usually concluded that the original epithelial character is lost and that the epithelium has been crowded out by an overwhelming intrusion of lymphocytes (immigration theory); others assert a direct transformation of the epithelium into leucocytes (transformation theory). Still others conceive that the thymus is not a lymphatic organ at all, but that the small lymphoid cells are epithelial cells according to their origin and remain such (pseudo-metamorphosis). Thus the views of different authors are much at variance although the immigration theory is constantly winning more ground.

Pl. 26, Figs 3–5

The lobules of the thymus (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II) show an outer CORTEX which is darker and in which the cells are closer together; and an inner, paler MEDULLA in which the cells are less crowded but are of greater size. Secondary nodules, such as occur in true lymphatic organs, are lacking in the thymus. The **cortex** consists of small cells like lymphocytes, closely pressed together, lying within a reticulum formed of anastomising cells. This reticulum has been produced differently from that of other lymphatic organs inasmuch as it is of epithelial origin and represents the remains of the original epithelial anlage of the organ. Within this purely cellular reticulum there are also to be found fibrillar structures which, at least in the immediate neighborhood of the numerous vessels of the cortex, are of a connective tissue nature (otherwise they would have to be epithelial fibers). The cells are very poor in protoplasm and have relatively large, round, basophilic nuclei (so-called small thymic cells or thymic cortical cells). They increase by mitosis and beside being transformed into true lymphocytes they certainly give rise to plasma cells which, with mast cells, are invariably found in the thymic cortex. They probably give rise to other forms of leucocytes as well.

Cortex and medulla are not sharply marked off from one another in the thymus, the explanation being that both are composed of essentially the same structural elements. In particular the thickness of the cortical zone is highly variable; for it often shows local thickenings related like secondary lobules to the main one and in such areas is of especial thickness. On the other hand it may be very thin, so that in some localities (base of the lobule) the medulla is entirely lacking and in others it almost reaches the interstitial tissue. During involution places where the cortex is absent are increasingly to be observed.

As regards the peculiarities of the structure of the **medulla**, in the first place the reticulum differs from that of the cortex in being formed of relatively large branched cells, containing a proportionately large nucleus. In spite of their branching, these reticulum cells of the medulla show their epithelial origin better than do the small reticulum cells of the cortex. Their descent from the epithelial glandular tissue of early embryonic life is still unmistakable. The medullary cells of the thymus are probably (p. 156) of lymphocytic origin like the small cortical cells; only in general they are larger and are not placed so close together. In addition mitotic divisions are much more rare in the cells of the medulla. Pl. 26, Figs. 3—5

An especial peculiarity of the medulla of the thymus is the invariable presence of structures which before all else are characteristic of thymus. These are the so-called HASSALL'S corpuscles, irregularly formed masses of epithelium which in part are often arranged in concentric layers. The corpuscles vary in size but in extreme cases may attain a diameter of $^1/_4$ or even almost $^1/_2$ mm. The smaller of these corpuscles, which are found in large numbers in the medulla of the fully developed thymus, are simple groups of flat epithelial cells. The larger corpuscles consist of a sort of capsule which is formed of several layers of flat, concentric cells. In the interior of the corpuscle are epithelial scales, usually non-nucleated and in part even cornified. Pl. 26, Fig. 5

Hassall's corpuscles appear during the third month of embryonic life, but usually do not attain their full size until later. They are present up to the time of involution without regressive processes being observed in them. Connected corpuscles, so-called twin formations, also occur. In the center of the larger corpuscles are often found homogenous, strongly staining masses of high refractive index, which probably represent cells that have undergone hyaline or colloidal degeneration. Scattered epithelial cells, not assembled in masses, also occur in the medulla of the thymus.

In the strands of connective tissue which separate the individual lobules there are found slender cords, medullary (or parenchymatous) cords, which join together the lobules, the so-called *tractus centralis*. Different varieties of leucocytes, including eosinophiles, wander out of the interstitial connective tissue into the gland; so that the latter invariably contains true colorless blood cells as well as the lymphoid cells of possible epithelial origin. The immigration occurs only in that part of the medulla which adjoins the connective tissue septa, not at all in the cortex.

The interstitial connective tissue is at first free from fat cells, particularly in the newborn and during infancy, at which time the organ is found at its highest development. In adults the connective tissue becomes increasingly transformed into adipose tissue which forces the lobules asunder and results in formation of the retrosternal fat body (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II). Pl. 26, Fig. 4

The thymus reaches its relatively greatest weight in the newborn, then quickly diminishes. However in all the early years of life it is a very important organ, increasing slowly in size even until the time of puberty, at which time growth ceases and actual involution very gradually begins. Nevertheless until the sixtieth year of life considerable remains of the organ may be found.

Pl. 26, Fig. 4 The process of involution is connected with the increase in adipose tissue described above and concerns the true parenchyme of the thymus and primarily the cortex. At the surface of the lobules the latter becomes constantly more uneven and its cellular elements diminish in number; while the medulla on the other hand is much less affected, the corpuscles of Hassell in particular continuing to increase and appearing especially large and numerous. As the bulk of the cortex diminishes, the medulla to an increasing extent comes to lie next to the interstitial adipose tissue. Finally in the senile thymus the cortex is completely absent.

As regards the BLOOD and LYMPHATIC VESSELS of the thymus, the former are very numerous. Quite a number of small arterial branches enter the organ and at first run longitudinally in the central tract to enter into the medulla of the lobules. From here they pass into the cortex which is much more highly vascular than the medulla. The blood flows away chiefly through large interlobular veins and by deep veins. Lymphatic vessels also are present in the thymus, but their relations are very different from those of the lymph glands. In particular they do not form a sinus but run courses similar to those of lymphatic vessels in true parenchymatous organs; that is to say they accompany the blood vessels, particularly arteries. Without doubt they appear to carry off the proliferation products of the thymic cortex.

Beside vasomotor nerves, fibers are also found in the thymus which enter the medulla independently and end there. Nerves have not been followed into the cortex.

III. Organs of the Muscular System

The organs of the muscular system comprise in the first place the muscles, tendons and fasciae and, occupying a secondary position, the tendon sheaths, bursae, etc.

The **muscles, musculi,** consist of numbers of striated muscle fibers which in general Pl. 27, Figs. 1, 2 lie parallel to one another and are marked off into distinct subdivisions by septa of connective tissue. The outer, more strongly developed connective tissue lying on the surface of the muscle is termed the *perimysium externum (epimysium)*. It sends into the interior of Pl. 28, Fig. 2 the muscle at irregular intervals, septa which bound muscle bundles of different sizes and which constitute the *perimysium internum*. Primary, secondary, and even tertiary muscle bundles may thus frequently be distinguished. Very delicate extensions from the perimysium internum surround each individual fiber within the bundles, so that the separate fibers as a rule are never in contact with one another by their sarcolemmal sheaths. However the connective tissue between the individual muscle fibers is often very scanty, although it carries the blood capillaries and the finest branches of the nerves. Often it appears to consist only of precollagenous reticulum fibers. In addition it is thought that, as set forth above (p. 61), the sarcolemma of the muscle fiber is itself of connective tissue nature, at least in the greater part of its thickness, so that is passes directly into the sparse connective tissue which separates the muscle fibers.

The perimysium externum is quite rich in elastic fibers; however the quantity of elastic tissue varies from muscle to muscle. The number of fibers composing a muscle bundle is highly variable, as is also the thickness of the fibers and the proportion between thin and thick fibers; nor is the amount of the perimysium constantly the same. Some muscles consist of coarse and others of slender bundles. At the points of intersection of the perimysium there lie the larger blood vessels and nerve trunks of the muscle (see below) and commonly muscle spindles. However, not all the muscles of the body contain muscle spindles; they are absent from the facial and ocular muscles (?) and from many other small muscles such as those of the pharynx, larynx, perinaeum, etc.

The **muscle spindles** are long fusiform structures lying in the long axis of the muscle Pl. 27, Fig. 2 and chiefly located near its central region. Each is surrounded by a stout sheath of perimysium which separates it from the muscle bundles proper. Within this sheath is a delicate concentric sheath of connective tissue containing muscle fibers which are usually very slender and which represent, as it were, a small muscle bundle. The muscle spindle is particularly rich in nerves. In contrast to ordinary muscle fibers the slender fibers of the spindle show many peculiarities. In particular they have centrally placed nuclei which are especially numerous midway along the course of the fiber. They are not closely associated with the ordinary fibers of the muscle but begin and end freely within the spindle sheath provided by the perimysium. The muscle spindles contain numerous nerves which show peculiar terminations (p. 179). It is most highly probable that they are sensory organs presiding over the muscle sense.

The BLOOD VESSELS of muscles are very abundant. The larger trunks run in the coarser septa of the perimysium and chiefly along the lines where the septa intersect. Branches from these trunks pass into the muscle bundles and each individual muscle fiber is surrounded by very slender capillaries which lie in the scanty reticulum around the muscle fibers where they form long meshes. The veins of the muscles contain many valves. The LYMPHATIC VESSELS have the same course as do the blood vessels but do not penetrate between the individual fibers.

The NERVES of the muscles are equally abundant; they are medullated fibers, some of which are motor and others sensory in function. The former end on the muscle fibers themselves, each muscle fiber usually containing several motor nerve endings (p. 177) and always at least one. The sensory fibers pass in part to the muscle spindles.

The **tendons, tendines,** are connective tissue organs. The greater part of a tendon consists of very regular and parallel bundles of connective tissue which contain very few elastic fibers and are termed tendon bundles (also tendon bundles of least size or primary tendon bundles). Each primary tendon bundle consists of a number of connective-tissue Pl. 27, Figs. 3, 4 fiber-bundles firmly cemented together and running a strictly longitudinal course. Between the bundles there are present clefts which probably contain a kind of cement substance by means of which the individual bundles are fastened together. In these clefts lie the Pl. 28, Figs. 1, 2 tendon cells which in the cross section of a tendon appear more or less stellate because of the processes projecting from the flat cell body. These processes extend for a distance into the clefts between the bundles of fibrils. However they do not fill the clefts completely, consequently they do not anastomose and surround the bundles on all sides. In general the form of the cell corresponds perfectly to that of the cleft in which it is situated. The cytosome of these tendon cells often shows troughlike impressions produced by the neighboring tendon bundles. The cell itself is elongated in a direction parallel to the Pl. 9, Fig. 2 long axis of the bundle and has a markedly elongated nucleus. The individual cells are usually arranged in distinct rows. In many tendons, for instance tendons from the tail of Fig. 10 a mouse, the individual flat cells of a row, which usually have an irregularly four-sided outline, follow one another so closely that only very narrow intervals separate the neighboring cells. The short processes which extend outward from the surfaces of the flattened cells penetrate for a distance into the clefts between the neighboring bundles and appear as winglike appendages of the body of the cell (so-called tendon wing-cells). The cells of the tendons of the human body, particularly of the larger tendons, are not only less numerous, but are less regular in form and arrangement (p. 66).

Each tendon consists of a number of tendon bundles held together by septa of loose connective tissue containing a considerable number of elastic fibers. The connective tissue Pl. 28, Fig. 1 which surrounds the tendon on the outside sends processes into the interior, forming septa which by their anastomoses separate irregular bundles of varying size and form; these constitute the so-called SECONDARY TENDON BUNDLES. The larger tendons contain a number — often a considerable number — of secondary tendon bundles.

Tendons are very poor in blood vessels, particularly in adults; during youth they are more richly vascularized. The blood vessels and their larger branches lie at the intersections of the anastomosing connective-tissue septa. On the other hand, the tendon is very rich in sensory nerves which go partly to the VATER-PACINIAN CORPUSCLES (corpuscula lamellosa), partly to other similar corpuscles (p. 181) and partly to the so-called TENDON SPINDLES (p. 179) which lie close to the junction between muscle and tendon. The finer nerve fibers are non-medullated and form delicate networks in the tendon.

APONEUROSES and FASCIAE have a structure similar to that of tendons. At least this is the case with the heavier fasciae, while the thinner fasciae resemble more in their structure that of the perimysium externum.

The TENDON SHEATHS resemble joints in structure; their inner surface, at least in part, bears a layer of endothelium. The BURSAE are rich in blood vessels and have a wall of very delicate connective tissue in which are many elastic fibers.

Pl. 28, Fig. 2 The connection between muscle and tendon is brought about essentially by the transition of the perimysium into the connective-tissue bundles of the tendon; but in addition a Pl. 13, Figs. 8, 9 direct passage of myofibrils into fibrils of the tendon may be demonstrated (p. 106). Short elastic tendons occur in situations where fine, isolated muscle fibers, or small groups of fibers, radiate into mucous membranes.

IV. Organs of the Nervous System

1. The Central Nervous System[1]

a. The Spinal Cord, *medulla spinalis*

Pl. 32, Figs. 3—5 The spinal cord is composed of two parts known respectively as the grey matter and the white matter (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III). The grey matter of the spinal cord is composed of much neuroglia with numerous nerve cells and many medullated nerve fibers which may be either isolated or in small bundles. All these Pl. 33 elements are much interwoven (see below). In addition the telodendria of other neurones are found terminating in the grey matter. The white matter consists of medullated nerve fibers without neurolemma, between which lies a relatively small amount of neuroglia. In addition, processes of the pia mater enter into the white matter. By far the greater number of nerve fibers of the white matter run strictly longitudinal courses within the columns of the spinal cord; the fibers of the anterior and posterior roots of the spinal nerves are the only considerable bundles which run in a transverse direction.

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[1] Here only the finer microscopic structure of the chief portions of the central nervous system will be set forth; for details see textbooks of descriptive anatomy and special books on the anatomy of the central nervous system. The general structure of the spinal cord is also explained but the variations in its structure from region to region are not dealt with.

The GANGLION CELLS, or better the **nerve cells**, of the spinal cord are, without exception, of the so-called multipolar type (p. 116) but of very different sizes. The largest cells are the MOTOR NERVE CELLS OF THE ANTERIOR HORNS, the **cellulae radiculares** of the official nomenclature. Their bodies have an average size of 70—140 μ. Usually they are arranged in several groups.[1] Their axones are directly continued, usually after giving off very fine collaterals, as the nerve fibers of the anterior or ventral roots.[2] The body of the cell is large. The dendrites arise by stout trunks from the bodies of the cells and send numerous branches even as far as deep into the posterior horns.

Pl. 32, Fig. 4

The remaining nerve cells of the grey matter of the spinal cord are smaller, most of them much smaller; their dendrites are very long[3] but are not so greatly developed or so numerous. Since their axones run in the tracts of the white matter, from which situation they give off collaterals at different levels into the grey matter, these cells, in contrast to the root cells, have been called the TRACT CELLS or **cellulae funiculares**. Some of them lie scattered in the grey substance while others are in groups. The DORSAL NUCLEUS, *nucleus dorsalis* or COLUMN OF CLARK, is such a group. It lies at the median side of the base of the posterior horn. It is well developed in the lower thoracic and upper lumbar regions of the cord, but is not altogether lacking in the remaining part of the dorsal and in the lower cervical regions of the cord.

The axones of the tract cells, having given off several collaterals, enter the white substance (usually the anterior or lateral tracts) of the same or of the opposite half of the spinal cord. Consequently the terms homolateral and contralateral are applied to the cells. The term commissural cells is not so good as the term contralateral, but was given because the axones run through the anterior grey commissure of the spinal cord. The cells are comparatively large and approximate the motor cells in size. They lie exclusively in the posterior median part of the anterior horn and in the middle region of the adjacent grey matter, never in the posterior horn.

The *substantia gelatinosa* (of Rolando) is formed of especially small tract cells and of small ganglion cells, all of which lie in abundant neuroglia.[4] Elongated fusiform cells, so-called marginal cells, lie in the reticular layer which bounds the substance of Rolando on its dorsal side, the so-called *stratum zonale* or *zona spongiosa*.

The axones of almost all the tract cells are medullated nerve fibers and run for a distance vertically in the spinal cord as ascending or descending TRUNK FIBERS, giving off on their way collaterals into the grey matter. The axones of the cells of the nucleus dorsalis on the other hand bend around into the dorsal lateral cerebellar tract in which they run cranially to the cerebellum.

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[1] Four groups are distinguished: 1. ventromedial, 2. ventrolateral, 3. dorsomedial, 4. dorsolateral In contrast to the tract cells, the motor cells of the anterior horns show a distinctly segmental concentration at the level of each nerve root.

[2] However a small group of nerve cells is found in the lateral horn, although not throughout the entire length of the cord (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III). These also represent root cells (of the so-called preganglionic fibers of the sympathetic nervous system).

[3] Many of the small scattered cells show forms which are markedly different from the polyhedral multipolar type of cell, certain of them can truly be termed fusiform.

[4] The substantia is thus by no means pure neuroglia. Delicate bundles of medullated nerve fibers traverse the substantia and give to it a finely striated appearance. These are collaterals (reflex bundles) of the posterior roots.

Beside these two varieties of nerve cells which belong to Deiters' type (Golgi type I, p. 116) there occur also in the posterior horns cells of the Golgi type II (p. 113) the so-called INTRINSIC CELLS of the cord.

Pl. 33 The nerve fibers of the grey matter present very complicated, and at first glance very irregular, relations. They traverse the entire grey matter partly as single fibers, partly in small groups, exceptionally in compact bundles of small size. According to their origin they are in part the beginnings of the motor roots and as such receive their medullary sheaths soon after leaving the bodies of their cells. In part they are fibers of the posterior roots, or collaterals from such fibers, which enter the grey substance through the posterior horns and pass on through the substantia Rolandi and the region of the dorsal nucleus into the anterior horns themselves, where they enter the region of the large motor nerve cells (reflex collaterals). Other collaterals serve to transmit the sensory stimulus in the so-called indirect sensory path and end, for example, with their telodendria about the cells of Clark's column.

The details of the course of the sensory root fibers through the grey matter of the spinal cord are somewhat more complicated than would appear at first glance. The fibers are the centripetal axones of the spinal ganglion cells (p. 118) which, combined as the posterior root fibers, have entered into the spinal cord. On entering the cord, usually a stronger median bundle may be distinguished from one which is weaker and lateral. The former passes through the posterior tract and enters the median side of the substance of Rolando. The latter on the other hand enters the apex of the posterior horn, not however the whole bundle but strong collaterals which are given off from it at right angles as the root fibers divide in T-like fashion;[1] while the bundle itself runs in the part of the white matter (posterior column and in part the stratum zonale, see above) adjacent to the grey matter. The stoutest collaterals of the median bundle pass through the median part of the substance of Rolando and represent primarily the numerous fibers of the reflex bundle running to the motor cells of the anterior horn.

In addition to the fibers of the anterior and posterior roots the grey substance of the spinal cord contains the terminations of the pyramidal tract from the brain (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III) and of other centrifugal tracts which enter into the anterior horn as medullated fibers from the pyramidal tracts and the corresponding areas of the anterior and lateral funiculi, and also of collaterals or terminations of the tract cells, which enter the grey matter.

The NEUROGLIA of the spinal cord shows in the grey matter all the principal types of its cells, ependymal cells, both long and short rayed astrocytes, and satellite cells. Special condensations of neuroglia are found surrounding the CENTRAL CANAL, the *substantia grisea* (gelatinosa) *centralis*. In this situation the ependymal cells and certain concentrically arranged astrocytes form a mass of glia which is completely free from nerve cells and almost devoid of nerve fibers. On the other hand the substantia gelatinosa posterior (of Rolando) contains nerve cells as well as abundant glia.

The ependymal cells surrounding the **central canal**, *canalis centralis*, which in adults as a rule is more or less completely obliterated, are cylindrical cells, ciliated during youth (p. 128), which are continued as glial processes, the so-called EPENDYMAL FIBERS. The glial elements of the grey matter form a dense feltwork (gliopil, see p. 129) in the meshes of which lie the true nervous elements, the nerve cells and nerve fibers.

Pl. 32, Fig. 4 The greater part of the **white matter of the spinal cord** consists almost exclusively of medullated nerve fibers of highly variable thickness, which run a longitudinal course. These fibers, like all others within the brain and spinal cord, have no neurolemma (p. 123). Occasionally isolated nerve cells are to be found in the white matter. Frequently in the white matter thin fibers and thick fibers are intimately mingled, but often whole parts of a funiculus will consist of fibers of almost equal diameter. The median portion of the posterior funiculus (the funiculus of Goll[1]) contains very fine fibers, while the neighboring funiculus of Burdach carries fibers which are clearly of somewhat larger diameter. Fibers of decidedly large diameter are found in many portions of the lateral funiculus (the lateral cerebellar tracts) and of the anterior funiculus.

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[1] The results of these divisions are known as TRUNK FIBERS; like their collaterals they finally come to an end after a course which, if ascending, is often very long; or which, if descending, is usually short.

Pl. 33

The nerve fibers which run longitudinally in the white matter of the spinal cord are in part axones from the cells of the cord (tract cells), in part fibers from the posterior roots, and in part axones from cells of the brain. Accordingly they may be divided into centripetal and centrifugal fibers. In addition the fibers vary greatly in length. Among the centrifugal tracts of great length are the pyramidal tracts running in the lateral and anterior funiculi, the fibers of which are axones from cells of the cerebral cortex. Centripetal fibers of the posterior roots fill the posterior funiculi, those from the lower roots lying always to the median side of the fibers which enter from the roots above. The axones of the cells of Clark's column form the dorsal lateral cerebrellar tract which like the posterior funiculi represents a long centripetal tract. The axones of the so-called commissural cells form the tractus[1] spino-thalamicus. The axones of the remaining tract cells form comparatively short tracts (ground bundles of the lateral funiculi, and the remaining parts of the anterior funiculi).

Beside the longitudinal fibers there are found in the white matter of the spinal cord a small number of fibers running transverse or oblique courses. These are fibers of the roots, collaterals which branch off at right angles from the longitudinal fibers to enter the grey matter and also fibers of the pyramidal and other tracts crossing in the anterior white commissure.

Apart from the nerve fibers the white matter is composed of neuroglia, almost exclusively of astrocytes whose long and slender rays are to be found between individual nerve fibers. A thicker layer of neuroglia, like a peripheral coat, covers the surface of the spinal cord and separates the nerve fibers from the pia mater (see below). Portions of ependymal fibers extend into the white matter; thus a part of the septum posterius and the bottom of the anterior median fissure are formed of ependymal fibers.

The large GANGLIA and most of the SMALLER NUCLEI OF THE BRAIN, as well as the CENTRAL GREY MATTER, are similar in structure to the grey matter of the spinal cord. They are composed of medullated nerve fibers, neuroglia and varying numbers of nerve cells, the latter usually being multipolar. In particular the ependyma of the ventricles of the brain is almost exactly like that of the central canal of the spinal cord. The microscopic structure of the medulla oblongata and of the entire brain stem continues that of the spinal cord, so that marked differences in the minute anatomical relations of these parts scarcely exist, variations are in general matters of regional position.[1]

b. The Cerebral Cortex

The cerebral cortex is primarily distinguished by the presence of nerve cells of a particular form, so-called **pyramidal cells,** which are characteristic of it alone. Moreover the other nerve cells present in the cerebral cortex are probably nothing but modified pyramidal cells; consequently the cerebral cortex (beside a series of smaller forms of cells which however are probably to be referred to the pyramidal cell type) contains only ONE essential variety of cell.

Pl. 28, Figs. 3, 4
Pl. 29, Fig. 3
Pl. 31, Fig. 1
Pl. 32, Fig. 1

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[1] For further information as to the structure of the spinal cord and medulla oblongata and as to the arrangement of their funiculi and tracts see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III.

Pl. 14, Figs. 2, 3, 4
Pl. 28, Figs. 3, 4

The pyramidal cells usually have three main dendrites proceeding from the corners of a pyramidal body, the apex of which forms an acute angle. The cell body is an extremely slender pyramid with a very narrow base. The axis of the pyramid is perpendicular to the surface of the gyrus. The chief or apical dendrite, which is also the longest, is a direct prolongation in the main axis of the pyramid. After giving off a few slender lateral branches it ramifies in the upper layer of the cerebral cortex (molecular layer), forming there its terminal arborization. The shorter, lateral (basal) dendrites are much less abundantly branched and spread out horizontally, that is parallel to the surface. The axone of the pyramidal cell leaves from its base and after a short course, during which it gives off collaterals, is continued into the white matter as a medullated nerve fiber.

Large, median, and small pyramidal cells are to be distinguished; occasionally, *e. g.* in the paracentral lobule, there are found particularly large cells, so-called giant pyramidal cells.

Fig. 19

The greatest length of the body of the small cells measures 10—15 μ.[1] These cells lie in the upper parts of the middle layer of the cerebral cortex (layer of small pyramidal cells, see below). The large pyramidal cells measure 20—30 μ and lie deeper than do the small cells (layer of large pyramidal cells). The giant pyramidal cells measure 80 μ and even more. In addition there are pyramidal cells of medium size. The smallest cells of the cerebral cortex are found in the so-called granular layer. Notwithstanding the very small size of these cells, which falls below 5 μ, they are essentially small pyramidal cells. In the deeper layers of the cortex, towards the medulla, there lie cells of various forms which are somewhat smaller than the large pyramidal cells and represent transitions from the latter to irregular multipolar cells, particularly to the so-called triangular cells. In these cells the ascending dendrite is poorly developed or quite lacking. They constitute the so-called POLYMORPHOUS CELLS. In the deeper parts of this layer the forms of the cells differ greatly from those above, fusiform cells often being present. Their axones however, like those of the pyramidal cells, pass into the medulla. In addition nerve cells of Golgi's type II (p. 113) are found in the cerebral cortex.

The cells of the cerebral cortex differ less in form than in size and are arranged in concentric layers in such fashion that each layer consists essentially of cells of the same size. In addition, layers in which cells are abundant alternate with others which contain fewer cells. A scheme such as follows is based on the stratified structure of the cerebral cortex.

At least six layers may be distinguished which are designated as follows proceeding from the surface of the cortex inward:

I. Molecular layer. It contains but few cells although it is not entirely free from them; on the other hand glia is abundant and the superficial tangential fibers run through it. The most superficial parts of the terminal arborizations of the chief dendrites from the pyramidal cells extend into this layer. The nerve cells of this layer, although few in number, are of varied form, some of them being triangular and others polyhedral.[2]

II. External granular layer. As already indicated this is usually a thin layer composed of very small pyramidal cells set very close together.

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[1] The difference in the measurements given for pyramidal cells depends upon the difficulty in determining the boundary between cell body and chief dendrite.

[2] The dendrites of these cells run for the most part in a horizontal direction. In addition under the name of CAJAL's cells there are described others said to have several (?) axones which take horizontal courses.

III. Layer of small and medium pyramidal cells. Usually this is very well developed and forms the thickest layer of the cerebral cortex. The cells are decidedly larger than those of the granular layer and are not so closely crowded together. The smaller cells lie toward the surface while the larger occupy the deeper parts of the layer.

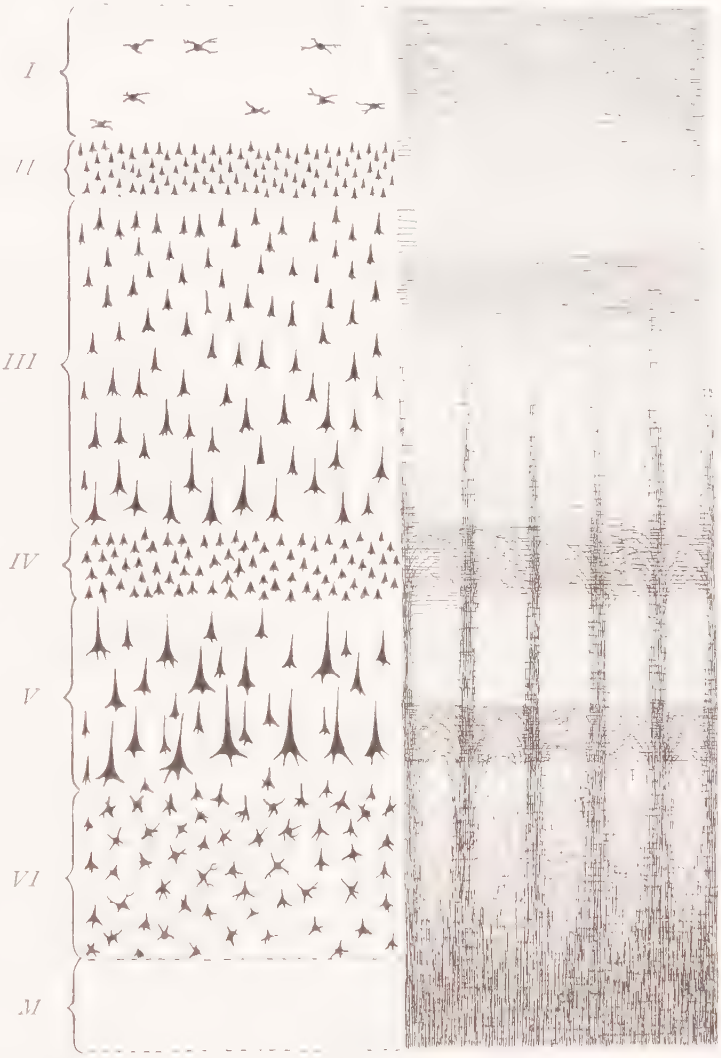

Fig. 19. **Diagram of the Structure of the Cerebral Cortex.**

The cells are represented on the left and the medullated fibers on the right.

I = molecular layer
II = outer granular layer
III = layer of small and medium pyramidal cells
IV = inner granular layer
V = layer of large pyramidal cells
VI = layer of polymorphous cells
M = medulla

IV. Inner granular layer. This, like the outer granular layer, is again a zone — and usually a narrow zone — of quite small pyramidal cells.

V. Layer of large pyramidal cells. This layer is usually not so broad as is the layer of small and medium pyramidal cells, but it contains the largest cells of this type, including the so-called giant pyramidal cells of many regions of the cerebral cortex. In accordance with their size, the cells lie relatively far apart. Although the large cells dominate the picture of the layer small pyramidal cells are always to be found scattered in between them.[1]

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[1] It must always be kept in mind that only the bodies, and not the long dendrites of the cells in question, are confined to the layers named, the separation of which from one another is more or less an artificial matter. For instance, the long apical processes of the pyramidal cells traverse several layers and extend even into the superficial molecular layer.

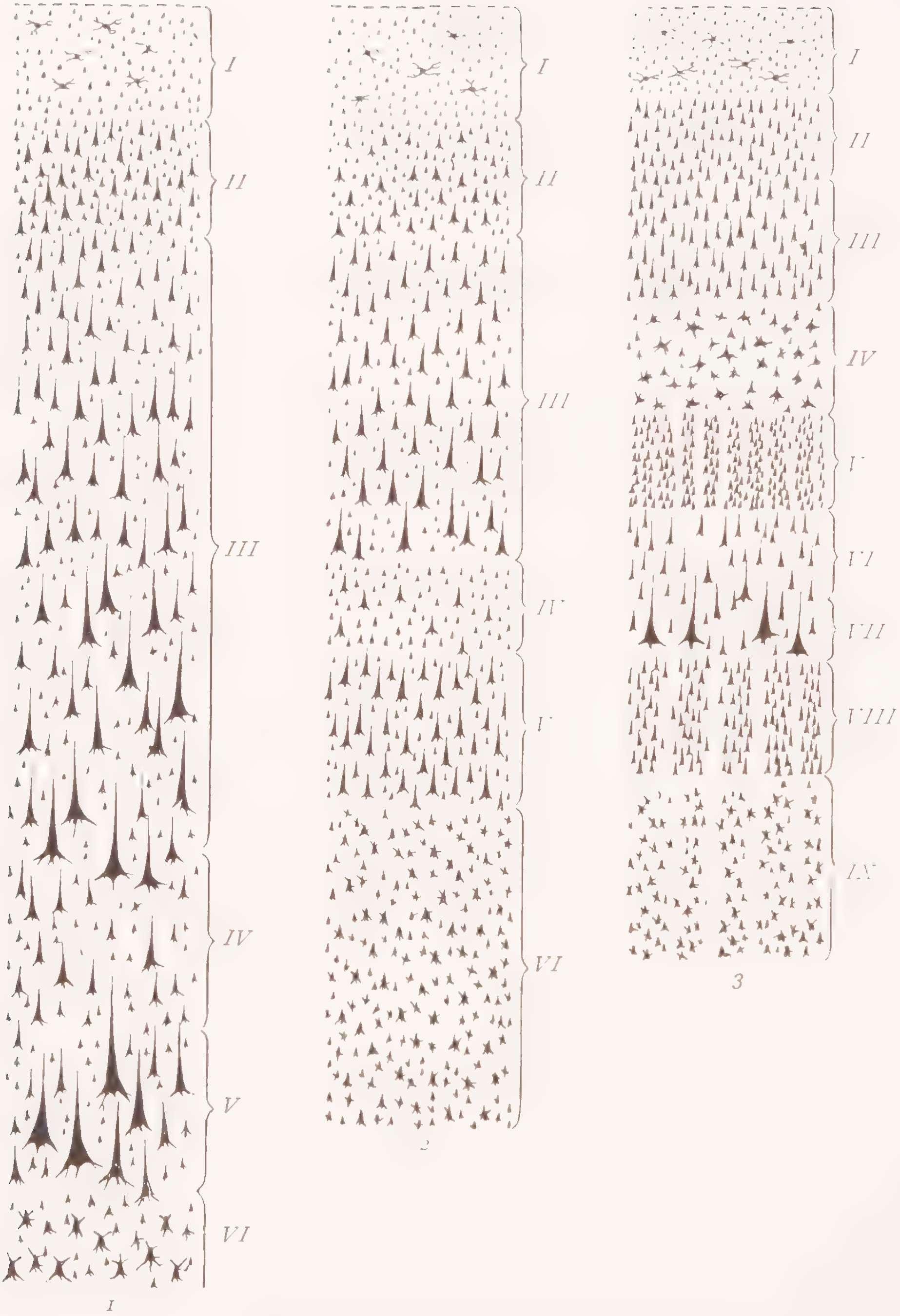
I
II
III
IV
V
VI
1
I
II
III
IV
V
VI
2
I
II
III
IV
V
VI
VII
VIII
IX
3

Fig. 20. **Cyto-architecture of the Cerebral Cortex.**

1 = Cortex of the anterior central gyrus
2 = Cortex of the superior temporal gyrus
3 = Calcarine cortex

In 1 and 2 the Roman numerals I—VI indicate the same layers as in *Fig. 19*. Note however that in 1 (anterior central gyrus) the number of pyramidal cells, particularly of the larger cells including the giant

VI. Layer of polymorphous cells. Here are situated those varieties of cells previously described as having irregular, spindle-shaped, triangular, or ovoid forms and as representing transitions between pyramidal cells and ordinary multipolar cells.

The manner in which the cells of the cerebral cortex are arranged varies in different regions: there is thus a CYTO-ARCHITECTURE of the cerebral cortex. The subdivision into Fig. 20 six layers which has been described above, may be taken as a starting point. This simple arrangement is seen most distinctly in the area of the posterior central gyrus.[1] In this locality the pyramidal cells are well developed, the granular layers are but poorly developed, although both are present. Still more simple is the structure in the psycho-motor region of the anterior central gyrus where the number of pyramidal cells is particularly great, and where giant pyramidal cells are constantly to be found. On the other hand, the granular layers are quite inconspicuous, indeed as a rule a true inner granular layer can no longer be distinguished because pyramidal cells are present in its territory. The cyto-architecture of the cerebral cortex is most elaborately developed in the calcarine region (visual cortex) in which nine layers may be distinguished; the number and size of the pyramidal cells is much diminished and small cells, in form like those of the granular layers, predominate. Large pyramidal cells are particularly few in number and appear in only a single layer in their much reduced stratum. The increase in the number of layers from six to nine is brought about essentially through a marked alternation of the larger and of the smaller varieties of cells (triple subdivision of the inner granular layer). In addition there are present here, as in other regions (cortex of the hippocampus), special forms of cells which in most cortical areas are lacking.

There are to be distinguished five different structural types in the cerebral cortex: 1. the AGRANULAR TYPE, recognized by the full development of pyramidal cells and the slight development, or complete lack, of the granular layers. This type is primarily found in the anterior central gyrus and also within the paracentral lobule and the parts of the two upper frontal gyri which are adjacent to the anterior central gyrus. 2. The so-called FRONTAL TYPE distinguished by granular layers which consist of very small pyramidal cells. This is the most common type of cerebral cortex and with the exception of the areas above named is most characteristic of the frontal gyri. It is found also in a part of the insula, within the superior parietal lobule, the precuneus and the anterior parts of the temporal lobe. 3. The PARIETAL TYPE, is characterized by well developed granular layers and small pyramidal cells and is found within the inferior parietal lobule, the gyrus supramarginalis and gyrus angularis and in the anterior parts of the occipital lobe.

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[1] The six-layer type of structure of the cortex is also the embryonic type and is at first present throughout the whole extent of the pallium; regional differences develop later.

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pyramids, is very considerable; that the granular layers are but slightly developed; that in 2, the layer of polymorphous cells is remarkably thick; also that pyramidal cells appear within the outer granular layer; that the layer of large pyramidal cells is thin and the cells themselves are not larger than are the largest of the medium pyramidal cells.

In *Fig. 3* the molecular layer is indicated by I; II indicates the external granular layer (well developed, with relatively large cells); III (scarcely to be distinguished from II) the superficial layer of small and medium pyramidal cells, the latter but few in number; IV the superficial layer of irregular polymorphous cells; V the inner granular layer (cells very small and numerous); VI the layer of larger pyramidal cells; VII a single layer of very large cells; VIII the deep layer of small pyramidal cells; and IX the deep layer of polymorphous cells.

4. The polar type, also known as the tenui-cortical type because of the thinness of the cortex and the relatively small size of all its cells. It is found in the neighborhood of the frontal and occipital poles whence the name. 5. The coniocortex, a thin cortex with very strongly developed granular layers, the cells of the remaining layers being very small. It is found in parts of the posterior central gyrus and parts of the temporal gyri, particularly the borders of the calcarine fissure and in a portion of the gyrus cinguli.

The **medullated nerve fibers** of the cerebral cortex in part extend radially as slender Pl. 29, Fig. 3 compact bundles (so-called medullary rays) from the medulla perpendicularly toward the surface of the gyri. They are in the first place the root fibers from both large and small pyramidal cells and from the polymorphous cells; and in the second place, sensory fibers and others of unknown origin which radiate into the cortex and there end. A not in- Pl. 29, Fig. 3 considerable proportion of the medullated fibers runs parallel to the surface of the gyrus Fig. 19 as the so-called tangential fibers. These fall into three chief layers; the most superficial of them forming the layer of tangential fibers proper. These lie in the most external part of the molecular layer close beneath the surface of the cortex and for the most part are but slightly developed; usually they are extremely fine fibers and like the following are branches of sensory fibers which have entered the cortex. The second layer is known as the super-radiary plexus, *i. e.* fine scattered fibers running parallel to the surface in the zone of the small pyramidal cells, and the upper part of the zone of the large pyramids. The medullary rays mentioned above extend only as far as this region and here in part become bent into a tangential direction. Both of these groups of tangential fibers stand in contrast to the much stouter, deep tangential fibers which, crossing the radial fibers, lie somewhat beneath the middle of the thickness of the grey cortex (in the deeper layer of the zone of large pyramidal cells and the zone of the polymorphous cells) and are formed of collaterals of the axones of the pyramidal cells. These constitute the so-called inter-radiary plexus. They form the line of Gennari which is often visible macroscopically and as the line of Vicq d'Azyr is especially well developed in the hippocampal gyrus and the gyrus fusiformis.

Just as there is a cyto-architecture of the cerebral cortex there may also be distinguished a myelo-architecture; that is, the relations of the cerebral nerve fibers also vary from one region to another. Particularly in the occipital cortex (calcarine region) the deep tangential fibers of the so-called internal band of Baillarger become thickened forming fine white lines visible in the grey cortex, the so-called lines of Gennari or of Vicq d'Azyr (see above).

The neuroglia of the cerebral cortex shows no peculiarities. Ependymal cells or fibers are not present in adults because of the great distance from the cerebral ventricles; although in the embryonic brain the ependymal fibers extend to the surface just as they do in the adult spinal cord. On the other hand both varieties of astrocytes are found, particularly those with short rays and distinct attachments to the walls of the blood vessels. Satellite cells are constantly found, particularly in the neighborhood of the large pyramidal cells.

c. The Cerebellar Cortex

Pl. 29, Figs. 1, 2 Considered macroscopically the cerebellar cortex consists of two sharply defined Pl. 30, Figs. 1—5 layers distinguishable by their color. Microscopically an intermediate third layer may be Pl. 31, Figs. 2, 3 distinguished. In contrast to the cerebral cortex, in which a subdivision into separate layers cannot be rigidly carried through, the individual layers of the cerebellum are sharply defined.[1] From without inward, they are named 1. the external grey or molecular layer, *stratum cinereum*, 2. the middle, ganglionic layer, *stratum gangliosum*, 3. the layer which is easily distinguishable, even macroscopically, by its different color, the granular layer, *stratum granulosum*. The latter layer borders on the medullary lamellae of the cerebellum (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III). All three layers contain nerve cells, and neuroglia; on the other hand nerve fibers are to be found only in the granular and ganglionic layers.

Pl. 29, Figs. 1, 2
Pl. 30, Figs. 1–5
Pl. 31, Figs. 2, 3
Fig. 21

The most peculiar of the cell forms of the cerebellum, and at the same time the largest, are the cells of Purkinje. Their bodies form the so-called ganglionic layer in which the cells occur in a single row between the granular and molecular layers. Their dendrites are extremely stout and are usually two in number, but there may be a single very stout dendrite which soon forks. The dendrites branch flatly like a trellis into extremely fine and closely set twigs which traverse the entire thickness of the molecular layer and reach the surface of the cortex; thus only the pear-shaped cell body lies in the stratum gangliosum.[2] The branches of the dendrites invariably occupy a plane which is transverse to the long axis of the gyrus.

Pl. 14, Figs. 5, 6

When the Purkinje cell lies at the summit of the cerebellar gyrus its two large dendrites emerge from the broad end of the pear-shaped cell body in such fashion as to form an acute angle. Towards the base of the gyrus the angle gradually widens to a right angle; and finally to an obtuse angle. As they arise from the cell the dendrites are thick but as they branch they naturally diminish in thickness. The axone emerges from the apex of the pear-shaped cell body on the side opposite the surface of the gyrus. It runs through the granular layer giving off collaterals, some of which are recurrent and as a medullated nerve fiber it enters the medulla of the cerebellum.

In addition to the dendrites of the Purkinje cells the molecular layer of the cerebellum contains two other varieties of cells, between which there are probably transitional forms. These two varieties are named basket cells and small cortical cells. Both are rather small nerve cells of the multipolar type. The basket cells (also termed large cortical cells) lie in the deeper part of the stratum cinereum near the bodies of the Purkinje cells. They have a long axone which takes a curved course in a sagittal plane, parallel to the boundary between granular and molecular layers, running at the level of the junction of the dendrites of the Purkinje cells with their cell bodies. Its terminal arborizations surround, as with a basket-work, the bodies and axones of the Purkinje cells, a single axone always being thus related to several Purkinje cells. The dendrites are but slightly branched and run towards the surface.[3] The small cortical cells, on the other hand, are distributed throughout the entire thickness of the stratum cinereum, although they are most numerous in the middle and external layers. They are always found in but relatively small numbers. Their axones have no relations with the Purkinje cells; and their distri-

Pl. 30, Figs. 1, 2
Fig. 21
Pl. 30, Fig. 5

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[1] In reality a sharp boundary exists only between the stratum cinereum and the stratum granulosum. The stratum gangliosum is not in itself a true stratum but belongs to the stratum cinereum.

[2] The entire mass of the dendrites thus form a moderately thick plate which has the form of a trellis. Recent investigations have shown that the arborizations of the dendrites of neighboring cells are continuous one with another.

[3] The baskets around the Purkinje cells are not formed by the axones of the basket cells alone, but the large granular cells also share in their formation as do also the telodendria of fibers ascending from the medulla. The baskets, which probably are complete networks without free nerve terminations, are also in connection with one another through fibers.

bution is not certainly known although they usually seem to branch quite close to the body of the cell from which they arise. The stratum cinereum is thus, in the main, a layer of neuropil.

The GRANULAR LAYER OF THE CEREBELLUM derives its name from its appearance under the microscope, an appearance produced by the numerous, small, closely set nerve cells which compose it. These cells are of two varieties which are intermingled and yet

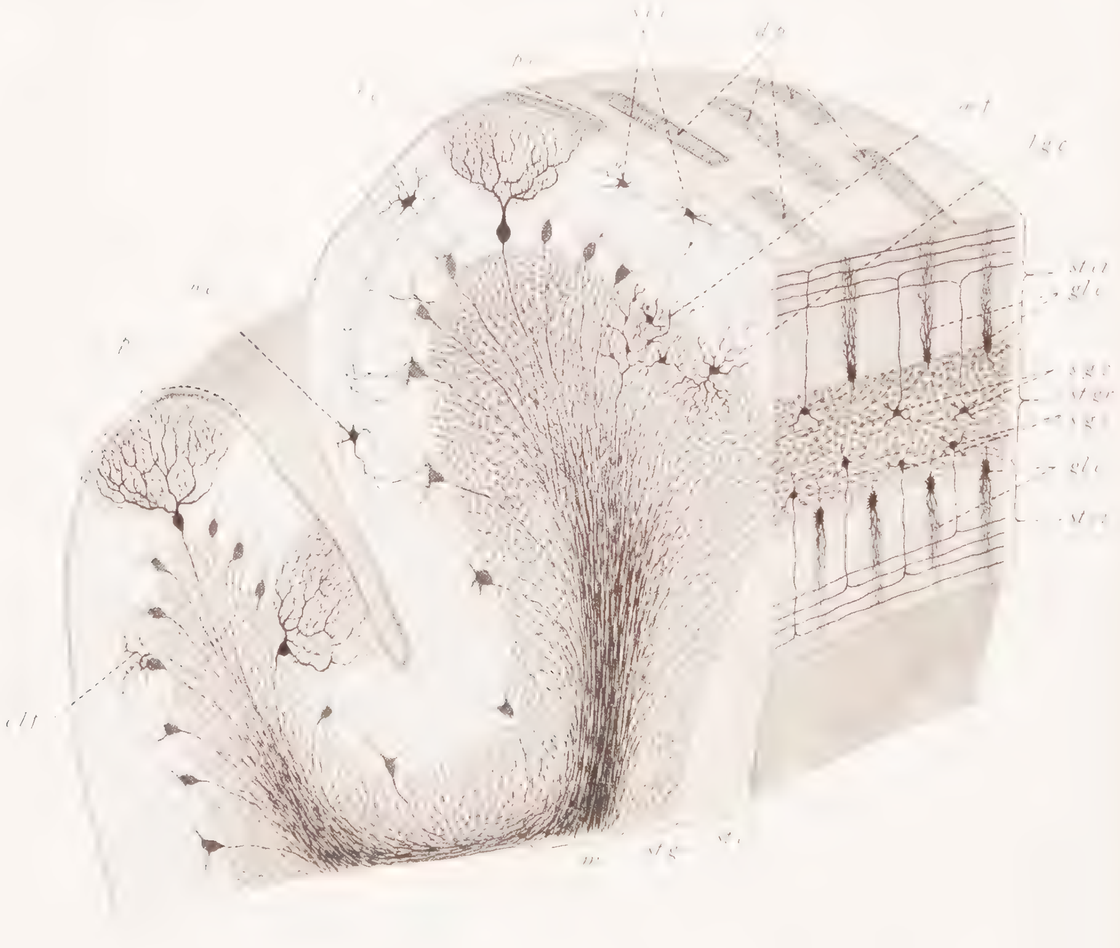

Fig. 21. **Diagram of the Structure of the Cerebellar Cortex.**

Portions of two neighboring gyri are represented, in transverse section, that on the right is also cut tangentially.

b c = basket cells
cl f = climbing fiber
d p = areas corresponding to the arborization of the dendrites of the Purkinje cells
gl c = glia cells
l g c = large granular cells
m f = mossy fiber
p c = Purkinje cell
s c c = small cortical cells
s g c = small granular cells
st ci = stratum cinereum
st gr = stratum granulosum
m = medulla

show a certain grouping. Large granular cells are to be distinguished from the small granular cells which constitute the greater part of the cellular elements of the layer. The former are cells of Golgi's type II, *i. e.* their axone arborizes within the stratum granulosum, in the immediate neighborhood of the cell, without having received a medullary sheath; while the dendrites extend into the stratum cinereum and there break up into branches. The small granular cells on the other hand are scarcely half the size of the larger, and are among the smallest nerve cells of the body (6—7 μ). In contrast to other nerve cells the relatively large nucleus is surrounded by only a narrow border of protoplasm. They have a few (2—5) short dendrites terminating in peculiar clawlike branchings. Their axones are medullated in the early part of their course which leads them perpendicularly into the upper part of the grey molecular layer. Here they divide in T-like fashion and continue parallel to the cerebellar surface (without further branching?). This course leads them in a frontal plane through the branchings of the Purkinje cells. Between the small granular cells, which are distinctly arranged in groups, there are left small intervals occupied by masses readily stained by eosin and consequently known as eosin bodies. Their significance is as yet unexplained (neuropil?).

Pl. 30, Figs. 1—5
Pl. 31, Fig. 3
Pl. 30, Figs. 1—3
Fig. 21
Pl. 31, Fig. 3

As regards the neuroglia of the cerebellum, in the white matter there are found chiefly long-rayed, and in the granular layer, short-rayed astrocytes; while in the molecular layer there are present both typical and modified short-rayed astrocytes (so-called Bergmann's cells), the cell bodies of which are found at the level of the Purkinje cells. Their long branches run towards the surface and there branch and terminate; while a few short processes also run downward into the granular layer. The expanded upper ends of these cells form a kind of superficial glial membrane. Satellite cells are also present.

Pl. 30, Fig. 2
Fig. 21

The **medullated nerve fibers** of the cerebellum form a dense plexus in the stratum granulosum, to which the axones of the Purkinje cells contribute the smaller part, the remainder being formed by fibers coming into the cortex from the medulla. The so-called climbing fibers reach the stratum cinereum and like vines follow the branchings of the dendrites of the Purkinje cells. On the other hand the mossy fibers, which are equally branched, terminate in the stratum granulosum. A number of these fibers appear to end in the eosin bodies. In addition, fibers proceed from the plexus in the stratum granulosum to the bodies of the Purkinje cells around which they form an interlacement on the side next to the granular layer. At the boundary of stratum granulosum and stratum gangliosum there lies parallel to the surface a narrow zone of medullated fibers, a few of which pass to the deeper parts of the molecular layer. In contrast to the condition in the cerebral cortex, the middle and outer portions of the molecular layer remain entirely free from medullated fibers.

Pl. 29, Figs. 1, 2
Pl. 30, Figs. 4, 5
Fig. 21

d. Hypophysis and Pineal Body

The **hypophysis,** *hypophysis cerebri*, must be included among the more or less rudimentary appendages of the brain, a classification which is peculiar because the organ consists of two lobes of very different structure and origin. However the lobes, unlike those of most organs, are not sharply marked off from one another externally. The larger, anterior lobe, *lobus anterior*, is epithelial and is derived from an evagination of the epithelium of the embryonic stomadeum; while the smaller, posterior lobe, *lobus posterior*, is developed from the brain.

Pl. 31, Fig. 4

Although the posterior lobe is a degenerated nervous organ, it never contains nerve cells but consists of a connective tissue framework with considerable neuroglia and scattered true nerve fibers which enter through the peduncle of the hypophysis. The anterior lobe functions as a gland of internal secretion and is composed of EPITHELIAL CORDS which form trabeculae of varying diameter and anastomose with one another. These trabeculae are invariably surrounded by numerous capillaries. At the boundary of the two lobules in addition to the solid cords of cells there are also found VESICLES like those of the thyreoid gland (p. 228) which often clearly contain COLLOID. This region constitutes the so-called intermediate lobe which in many animals is well developed and sharply separated from the anterior lobe. The epithelial cells of the hypophysis are strongly oxyphilic and commonly show numerous well stained granules. These are termed chromophile cells; other cells, chromophobe cells, are present which do not contain stained granules. The organ belongs among the glands of internal secretion.

The classification of the epithelial cells of the anterior lobe of the hypophysis into chromophobe (chief) and chromophile cells, or into basophile and oxyphile cells has been emphasized by many authors but is probably only an expression of different functional states. However recently the fundamental difference between the two types of cells has again been urged.

The **pineal body,** *corpus pineale, epiphysis*, consists essentially of neuroglia although Pl. 31, Fig. 5 scattered nerve cells have been found within it. The pineal body is mainly an organ of internal secretion similar to the anterior lobe of the hypophysis, which it resembles in being formed of masses of epithelial cells. These cells, which probably form an internal secretion, are derived from the nervous anlage and represent embryonic nerve cells not yet specificially differentiated. In the adult, groups of these cells may be distinguished, being separated by connective tissue which is rich in glia. The cells have relatively large nuclei; their protoplasm may contain granules, some of which may be pigment granules. The glia fibers, which are abundantly present in the intervals between the connective tissue cells, enter also between the epithelial cells. There is found as a rule in the adult Pl. 30, Figs. 7, 8 pineal body the so-called brain sand, *acervulus cerebri*. This consists of small rounded concretions, *corpuscula arenacea*, which are formed of concentric layers of calcium carbonate and have an irregular form like that of a mulberry. In the connective tissue between the groups of epithelial cells there are found large numbers of mast cells.

The pineal body is somewhat different in structure during youth. It then consists of cords of cells connected in netlike fashion, in which clear, inner cells with abundant protoplasm and weakly stained nuclei may be distinguished from smaller, external cells whose nuclei stain strongly. The one variety of cell grades into the other. Brain sand has not yet appeared in the pineal body during youth. Its occurrence as a rule is to be considered an accompaniment of the degeneration of the organ, although degenerative processes worthy of the name are not to be found. The quantity of epithelial tissue is still very considerable in the adult.

e. The Membranes and Blood Vessels of the Central Nervous System

The central nervous system has three sheaths or membranes: 1. externally, the dura mater, *dura mater cerebralis s. spinalis*, 2. the middle membrane, the *arachnoidea* 3. internally, the *pia mater* (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III). The dura mater cerebralis is distinguished from the dura mater spinalis by the fact that it also represents the periosteum of the inner surface of the cranium. It consists consequently of two layers, of which the outer, periosteal layer is rich in blood vessels; while in the dural layer proper blood vessels are much less abundant. On the other hand it contains an abundance of nerves, not merely vaso-motor nerves but also separate, sensory nerves which terminate in the membrane itself. The dura mater is formed of dense connective tissue and has a covering of endothelium on its inner surface. Essentially it consists of interwoven collagenous fiber bundles in addition to which there are present numerous elastic fibers of very small diameter.

Since the dura mater also plays the part of an internal cranial periosteum it has on its outer surface a more or less complete layer of osteoblasts. The inner layer is less markedly fibrous than the outer and may occasionally become quite loose in texture, as in the immediate region of the wall of the sinuses where the arachnoidal villi penetrate into the dural tissue. Frequently the number of elastic fibers in the inner layer is much increased and forms a compact layer close under the endothelium.

The ARACHNOIDEA consists of delicate connective-tissue bundles which are arranged to form anastomosing trabeculae, and have a delicate elastic sheath as well as a covering Pl. 31, Fig. 2 of endothelium-like cells (p. 65). Of similar structure are strands which connect the pia mater with the arachnoidea. The external surface of the latter bears an endothelium similar to that which covers the inner surface of the dura mater. The PIA MATER consists of lamellar connective tissue and is closely applied to the substance of brain and spinal cord. It sends into the latter organs processes which contain blood vessels and which thus frequently bring about a firm union between its deeper layer and the nervous substance (spinal cord, brain stem). It carries the blood vessels and also contains nerves (see below).

The *telae* and *plexus chorioidei* are especially rich in blood vessels which form vascular loops held together by a small amount of connective tissue. Where the blood vessels project into the ventricles of the brain the **ependymal epithelium** is closely applied to the Pl. 30, Fig. 6 vascular loops. Its cells have a cubical form, are of typical secretory nature, *e. g.* they display granules, and may contain pigment and other inclusions. Only the thinnest possible layer of connective tissue separates the ependyma from the wall of the capillaries of the plexus. The cells of the ependyma secrete the *liquor cerebrospinalis internus*. The vascular plexuses contain brain sand.

The **blood vessels** of the central nervous system, as a general rule, are extremely abundant in the grey matter, but in the white matter are comparatively few. The arteries pass from the pia mater into the substance of the central nervous system while the venous trunks after emerging from the brain run in the pia mater. The vessels of the brain are surrounded by delicate perivascular sheats of connective tissue. On the other hand the capillaries lie free in the neuroglia, the processes of the astrocytes being connected with the capillary wall (p. 129).

Since the grey matter of the spinal cord is situated in the interior of the organ, the blood vessels in order to reach it must enter from the bottom of the median fissure. Thus the chief arterial branches extend with the pial lining of the fissure as far as the grey Pl. 32, Fig. 3 commissure from which position they pass right and left to the anterior horns. In this Pl. 33, Fig. 1 manner the grey matter of the spinal cord receives its chief blood supply but in addition quite small arterial branches from the pial plexus enter into the spinal cord by means of the septa of pia mater. These branches chiefly go to form the wide-meshed capillary network of the white matter. Frequently however a number of these small arteries extend into the grey matter and there, along with the chief arteries mentioned above (so-called central arteries), form the small-meshed capillary network of the grey matter.

Pl 31, Fig 2

In those regions of the cerebrum and cerebellum where the grey matter lies superficially and forms the cortical layer, fine arteries pass directly from the pia mater into the gray matter and after vascularizing the cortex as they pass through supply the white matter which lies beneath. Where large masses of grey matter, such as the large central ganglia, lie in the interior of the brain their blood supply is provided by definite arterial branches which enter through corresponding openings (true vascular canals) in the ganglia (substantiae perforatae). In situations where the white matter forms the outer surface of the brain the relations of the blood vessels are quite similar to those in the spinal cord.

Except for slight differences in the spinal cord the veins of the central nervous system show the same relations as do the arteries.

Of the MEMBRANES of the central nervous system only the dura mater possesses a blood supply of its own, which however is by no means abundant. The arachnoidea and pia mater have no vascular supply of their own, a circumstance particularly noticeable in the arachnoidea. The blood vessels contained in the pia mater do not form capillaries within the latter but vascularize solely the brain substance which is covered by the pia, not the pia itself. The small arteries which enter brain or spinal cord from the pia mater are terminal arteries.

LYMPHATIC VESSELS are not present in the central nervous system, but their place is taken by LYMPHATIC SPACES. These are 1. very narrow subdural spaces found between the arachnoidea and the dura mater, 2. the subarachnoidal space between the arachnoidea and the pia mater. The latter space is relatively wide and contains the *liquor cerebrospinalis externus*. In addition the spaces between the blood vessels and their sheaths are probably lymphatic spaces.

NERVES are present in all the meninges, as sympathetic nerve fibers supplying the smooth muscle of the blood vessels. But in this connection it must be noted that the cerebral vessels, including the arteries, contain remarkably little muscle and within the central nervous system the blood vessels are devoid of nerves. In addition both dura and pia mater contain medullated sensory (?) nerve fibers which are found partly in the form of terminal networks and partly, at least in the pia mater, as terminal corpuscles (of Meissner). The telae chorioideae and vascular plexuses are particularly rich in nerves.

As to the nerve supply of the pia mater the following details are to be noted: the abundant vasomotor nerves of the arteries are derived not merely from the sympathetic but also from the parasympathetic system and form networks in both the muscular and adventitial coats. Loops and terminations are also to be found upon the walls of the capillaries.

Moreover the pia mater, in addition to small nerves coming directly from the cranial nerves (especially from cranial nerves X and XI), contains also, at least in the region of the brain, nerve cells, which in turn give off nerve fibers. The corresponding nerves of the pia mater spinalis arise in part from the posterior roots and in part from the vasomotor nerves which always contain medullated fibers. Nerve endings although few in number are also to be found in the pia mater spinalis.

2. The Peripheral Nervous System

The peripheral nervous system is composed of: a, the peripheral nerves; b, the peripheral ganglia; c, the peripheral nerve terminations.

a. The Peripheral Nerves

The peripheral NERVES of the CEREBROSPINAL system consist essentially of medullated nerve fibres (p. 123) which, along with certain non-medullated fibers, are embedded in connective tissue and not in neuroglia as in the white matter of the central nervous system. Within the sympathetic nervous system most of the fibers lack the medullary sheath.

Every peripheral nerve consists of a variable number of separate FUNICULI, *i. e.* of cylindrical cords formed of groups of medullated nerve fibers. Even within the same nerve the funiculi may vary greatly in size and each individual funiculus is surrounded by a connective-tissue sheath, the PERINEURIUM. This consists of concentric lamellae of connective tissue with a few layers of flat cells and fine, but numerous, elastic fibers. Clefts often occur between the lamellae and are lined with flat endothelium-like cells. Pl. 35

Processes proceed from the perineurium into the interior of the funiculus and form an irregular network known as the ENDONEURIUM which, at least in the larger funiculi, mark off rather irregular bundles of a lower order. Each individual nerve fiber receives from the endoneurium a delicate sheath, the so-called FIBRILLAR SHEATH OF HENLE[1] or ENDONEURAL SHEATH. This is formed of delicate fibers but often appears almost homogeneous; as a rule, but not invariably, it contains nuclei. Within the funiculus almost all the nerve fibers are medullated and run longitudinally, except at points where branches are given off, or where communications occur between bundles. These communications are very abundant and always take place at very acute angles (so-called internal plexus).

Each nerve of larger size consists of a number of funiculi of varying diameter held together by loose connective tissue which commonly contains fat and an abundance of elastic fibers. This connective tissue is continued as a sheath around the entire nerve and is named the EPINEURIUM. As mentioned, it commonly contains adipose tissue and always carries the chief blood vessels of the nerve.

The SYMPATHETIC NERVES are distinguished from the cerebrospinal nerves chiefly by containing numerous non-medullated fibers along with a very few, medullated fibers which usually are very fine and are partly of cerebrospinal origin. However the proportion between the numbers of the two kinds of fibers often varies considerably in different sympathetic nerves. In man large sympathetic nerve trunks, particularly those which consist of several funiculi, are rare.

The peripheral nerves are relatively poor in blood vessels, the larger vessels lying exclusively in the epineurium; while the capillaries penetrate into the endoneurium. As in the central nervous system, lymphatic vessels are absent. Nerves (nervi nervorum) are usually found upon the walls of the blood vessels and perhaps also in the connective tissue (?).

b. The Peripheral Ganglia

These are subdivided into α, cerebrospinal and β, sympathetic ganglia; along with the latter being included the so-called paraganglia. The former occur only on the posterior roots of the spinal nerves and on the corresponding cranial nerves (n. trigeminus, n. vagus, n. glossopharyngeus, ganglion semilunare nervi trigemini, ganglion geniculi partis intermedii n. fascialis).

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[1] To name this sheath after Henle is really an error.

A ganglion is a collection of a number, usually of a considerable number, of nerve cells of definite type (p. 118) forming a compact body, usually surrounded by a connective-tissue sheath and lying within the bounds of the PERIPHERAL OR OF THE SYMPATHETIC NERVOUS SYSTEMS.

In the sympathetic nervous system (p. 177) there are all transitions between sharply defined ganglia and smaller, scattered groups of nerve cells, hemiganglia.

α. The Cerebrospinal Ganglia

Pl. 34, Figs. 1, 2 The CEREBROSPINAL GANGLIA have a firm covering of connective tissue which is a continuation of the dura mater and which sends connective-tissue processes into the interior of the ganglion, ensheathing the bundles of nerve fibers and forming the CAPSULES Pl. 34, Figs. 1, 2 of the nerve cells. These capsules consist of a few concentric layers of connective tissue Pl. 15, Figs. 1—3 containing flat cells and surrounding a spherical space lined by a structureless mem- Pl. 16, Figs. 2—4 brane which contains the equally spherical ganglion cell. Within the membrane, that is to say on the inner face of the capsule or on the surface of the cell, there lies a single layer of flat cells, the continuation of the cells of Schwann (lemnocytes) from the neurolemma of the nerve fiber. These cells are not of connective-tissue origin but are derived from the ectoderm and are called amphicytes (p. 119). The ganglia of the sensory nerves named above are like the spinal ganglia in structure as are also the ganglia of the n. vestibularis and n. cochlearis whose nerve cells are bipolar (p. 119).

In addition to the sensory root fibers which break up within the ganglia into smaller and smaller groups before they connect with their nerve cells, there are present also non-medullated nerve fibers of sympathetic origin which enter the ganglion through the ramus communicans (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III) and wrap their terminal expansions around the cells of the spinal ganglia. Whether afferent medullated (cerebrospinal) fibers are present is doubtful.

Even in a hasty examination of a section through a spinal ganglion the nerve cells Pl. 34, Fig. 2 are seen to be of different types. Along with the predominating cells of medium size there are a few cells somewhat larger but otherwise very similar. In addition there are seen a considerable percentage of very decidedly smaller cells whose protoplasm stains much darker than that of the larger cells. There are doubtless further subdivisions of these types. A proportion of the cells last mentioned certainly belong to the sympathetic nervous system, a few cells of which are situated within the spinal ganglion. Moreover the cells of the ordinary sensory neurones and those of the visceral sensory neurones also seem to differ from one another. Further information as to the cells of the human spinal ganglion is lacking. The relations in animals are to some extent different from those in man.

β. The Sympathetic Ganglia

The majority of the sympathetic ganglia are surrounded by a connective-tissue sheath. They contain so-called multipolar ganglion cells which are often binucleate and Pl. 34, Figs. 3, 4 frequently are pigmented. They so far resemble cells of the spinal ganglia as also to lie Pl. 15, Figs. 5, 6 within connective-tissue capsules (p. 121).

In general the cells of the sympathetic ganglia are not situated so close together as are those of the cerebrospinal ganglia. Usually cells and non-medullated nerve fibers in larger or smaller groups are intermingled, and in general this relationship obtains largely throughout the sympathetic nervous system.

The sympathetic ganglia almost invariably contain medullated cerebrospinal nerve fibers which either may pass through the ganglia without entering in any way into connection with its elements; or after losing their medullary sheath may come into relation with the motor cells of the ganglion (fibers of the parasympathetic system and free ganglionic fibers), and surround them with their terminal arborizations. Whether non-medullated fibers of sympathetic origin may behave similarly in order to establish connections between ganglia above or below, is questionable, considering the peculiar features of the axones of sympathetic nerve cells (p. 120).

Often there are found very tiny sympathetic ganglia consisting of only a small number of cells, or even a small group of sympathetic nerve cells lying along the course of a nerve (hemiganglion). Frequently networks or plexuses of very regular construction are formed, in which groups of ganglion cells are located, Pl. 37, Fig. 1
usually at the points of intersection; while the nerve cords connect the neighboring ganglia. Such plexuses are common in many of the viscera and are of most typical form in the digestive tract (plexus myentericus and plexus submucosus see p. 212).

In addition to the cells which are typical for sympathetic ganglia there are present in certain parts of the body the so-called CHROMAFFINE cells, as found in the PARAGANGLIA. These cells have the appearance of epithelial cells but stand in intimate connection with the sympathetic nervous system. They have received their name from the fact that they are stained yellowish brown by treatment with chromic acid or with salts of chromium. The largest mass of these cells is represented by the medulla of the suprarenal gland (p. 259). The carotid gland (p. 260) and a few smaller bodies within the peritoneal cavity Pl. 70
also consist of chromaffine cells.

c. Peripheral Nerve Terminations

The terminations of the peripheral nerves comprise α, terminations of centrifugal fibers, which may again be subdivided into motor endings and secretory endings; β, sensory terminations of the centripetal fibers. The former show decidedly more simple features than do the latter.

α. Motor Nerve-endings

The nerves of the STRIATED muscles branch and anastomose within the perimysium. Not only are the nerve trunks themselves divided but the individual fibers branch as well, Pl. 36, Fig. 3
the number of the latter is greatly increased within the muscle itself. To each fiber of striated muscle there now runs at least one nerve fiber, and to long muscle fibers, several. Just before reaching the sarcolemma the nerve fiber loses its medulla but retains its neurolemma. The axis cylinder still covered by the sheath of Schwann now penetrates the sarcolemma and spreads out in the superficial sarcoplasm of the muscle fiber in the form of the so-called **motor end-plate.** This consists of a flat, oval, elongated mound of finely granulated material, termed the sole-plate, which lies immediately beneath the sarcolemma and contains antlerlike branchings of the axis cylinder, the ends of which appear thickened and clubbed. Recent investigations show that the axis cylinders never end freely; such appearances in gold chloride preparations are deceptive and are the result of incomplete impregnation. With the aid of special stains for neurofibrils it may be shown that the expansion of the nerve in the sole-plate consists of nets and rings which are formed by fine networks of the neurofibrils from the axis cylinder. These networks of neurofibrils in the sole-plate do not however represent the terminal branchings but are connected with a reticulum of delicate fibrils lying in the sarcoplasm around the muscle fibrils (see below). In addition at least one accessory, non-medullated, sympathetic fiber runs to each end-plate. In the sole-plate there are found a number of vesicular nuclei which are to be considered as neurolemmal nuclei; while the sole-plate itself prob-

ably consists of neuroplasm. From the network of neurofibrils in the end-plate there proceeds a delicate periterminal network which extends into the sarcoplasm and thus reaches the immediate neighborhood of the contractile substance.[1]

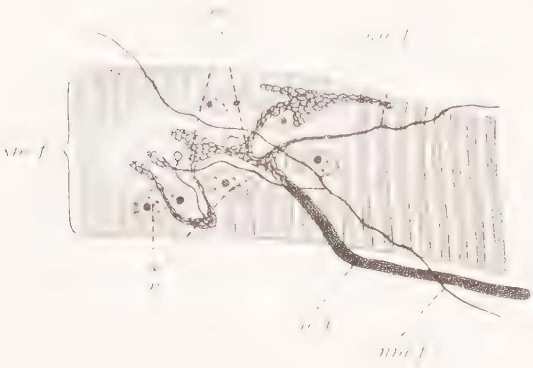

Fig. 22. **Diagram of the Innervation of a Striated Muscle Fiber** (after Boeke).

A thick, medullated cerebrospinal fiber and a thin, non-medullated fiber are both seen to reach the striated muscle fiber and participate in forming the fibrillar network of the sole-plate. An additional non-medullated fiber forms a separate network by means of a collateral.

m f = medullated fiber
n = nuclei of end-plate
net = network of neurofibrils
nm f = non-medullated accessory fiber
sm f = striated muscle fiber

As regards the motor endings of cardiac muscle and those of smooth muscle it was considered until recently that the non-medullated sympathetic nerve fibers of these types of muscle extend merely to the surface. It is now known that the nerve fibers enter into the interior of the elements of cardiac muscle, the neurolemma being continuous with the sarcolemma, while the neurofibrils extend into the perinuclear mass of sarcoplasm.

In the innervation of smooth muscle it has also been shown that the finest nerve terminations extend into the protoplasm of the muscle cells, and there end in eyelet-like structures or form entire networks of eyelets. Such non-medullated, sympathetic fibers come usually from nearby cells of intra- or inter-muscular plexuses, *e. g.* from those of the stomach wall.

The terminations of the centrifugal, SECRETORY nerves are also relatively simple. These terminations are entirely free like those of smooth muscle. The termination may be partly epilemmal, that is on the surface of the membrane propria, partly hypolemmal, that is to say the most delicate nerve terminals may penetrate the membrane and end between the gland cells themselves.

β. Sensory Nerve-endings

This group includes a very great variety of nerve endings but two chief categories may be distinguished: 1. free endings; 2. endings with terminal corpuscles. The spindles of muscles and of tendons constitute an intermediate type.

The FREE NERVE ENDINGS are found chiefly in epithelium, particularly in stratified
Pl. 36, Fig. 1 epithelium, but also in connective tissue membranes, in the capsules of joints and in the
Pl. 37, Fig. 3 connective tissue of muscles. Before entering into epithelium, for instance that of the

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[1] Since the nuclei of the sole-plate are beyond doubt neurolemmal nuclei, the neurolemma can not possibly fuse with the sarcolemma at the entrance of the nerve fiber, otherwise the nuclei of the sole-plate must be considered as belonging to the muscle fiber and the sole-plate be formed of sarcoplasm as some maintain. However, the motor end plate is definitely "hypolemmal" and not, as formerly thought "epilemmal". The name ultraterminal fibers has been given to delicate nerve fibers which arise from the expansion of the motor end-plate and run independently to another and neighboring fiber.

cornea or the epidermis, the nerve fibers lose their medullary sheath; consequently only the naked axis cylinders enter the epithelium, which they often penetrate even as far as the superficial layers. They terminate between the epithelial cells in slender points or buttonlike thickenings (cornea, epidermis, stratified pavement epithelium of mucous membranes).[1] In the connective tissue between muscle fibers there are free nerve-endings similar to those just mentioned. Direct nerve terminations have been demonstrated on the cells of connective tissue, for instance in the substantia propria of the cornea. Frequently, as in the cornea, the nerve fibers form plexuses before giving rise to their terminal branches. As in the case of motor nerves, so in these endings also, the neurofibrils usually form NETWORKS.

Muscle and Tendon Spindles

The spindles of muscles and of tendons represent endings of the SENSORY, centripetal nerve fibers of muscles. They occupy, as was mentioned, a position midway between free endings and those with terminal corpuscles; but incline, particularly in the case of tendon spindles, rather towards the free manner of ending.

TENDON SPINDLES are found within tendons close to the tendon-muscle junction. Pl. 36, Fig. 6
They are formed by a medullated fiber which enters the tendon, its fibrillar sheath blending with the connective tissue of the latter. The remainder of the fiber passes into a dense and very elaborate terminal branching within a narrow circumscribed space. The finest branches of the termination are, strictly speaking, only the simple terminations of the axis cylinder.

The spindles of RUFFINI found in the subcutaneous tissue of the fingers and in the bed of the nails, in submucous tissues and also in the myocardium etc. are very similar to the tendon spindles. They are formed of closely packed terminal branches which run upon and around spindle-shaped masses of connective tissue similar to those of tendon spindles.

The form and structure of MUSCLE SPINDLES have, in the main, been already described Pl. 27, Fig. 2
in connection with the muscles (p. 159). Beyond doubt they are sensory organs presiding Pl. 36, Fig. 7
over the muscular sense. Here it is sufficient to describe the relations of the nerve fibers and their endings. Into each muscle spindle there enters a small nerve consisting of a few medullated fibers, and as it penetrates the connective-tissue sheath of the spindle its fibrillar sheath fuses with the latter (p. 159); while the fiber, passing into the cavity of the spindle, loses its medulla. Occasionally several fibers enter the same spindle independently. The fibers having lost their medulla usually surround the muscle fibers of the spindle in spirals before breaking into numerous, closely packed, flowerlike, terminal branchings. These terminations are epilemmal, in contrast to the motor terminations which are also present in the muscle fibers of the spindle. At the same time the nerve terminations are surrounded by processes of the connective-tissue cells which they also innervate.

The **terminal corpuscles** appear under many forms; probably all the different varieties of these structures are not yet fully known. They fall into two groups: 1. terminations in connection with tactile cells; 2. terminations in the form of end bulbs.

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[1] In the epithelium which covers the nose there have been described in many animals two varieties of intra-epithelial nerve endings; first, those with small expansions and lateral branches which terminate upon the epithelial cells. Second, very thin fibers the course of which is marked by the formation of many small varicosities between the epithelial cells, and which form pericellular fibers after the fashion of the tactile cells of MERKEL.

1. Tactile Cells and Tactile Corpuscles

Tactile cells are found as SINGLE cells and also in tactile corpuscles. The former have an intra-epithelial position and are found in the deeper layers of the epidermis[1] and also Pl. 37, Fig. 2 in the superficial layers of the corium of the skin. They consist of a somewhat modified epithelial cell of medium size (ca. 10 μ) with a large vesicular nucleus, and of a tactile meniscus, that is of a saucer-shaped disc which contains delicate fibrillar nerve terminations and is applied to the tactile cell by its concave surface. In addition the terminal expansion of another fiber is applied to the exterior of the meniscus.

A tactile corpuscle consists essentially of a nerve termination proper surrounded by sheaths in the formation of which the adjacent connective tissue plays the chief part; although parts of the nerve fiber, the neuroplasm and the neurolemma, also share in its formation.

The simplest form of **tactile corpuscle** is represented by the CORPUSCLES OF GRANDRY. Pl. 37, Fig. 7 These are much larger structures (about 50 μ) than are the simple tactile cells. They consist of a row of from two to five large flat cells (about 15 μ thick),[2] with abundant protoplasm and relatively small vesicular nucleus. In the central parts of the protoplasm of the cell there may be demonstrated peculiar curved fibrous structures running transversely to the long axis of the cell. These cells are probably elements of connective tissue origin; however the conception that they represent neurolemmal elements is very reasonable. There is also an intimate connection between the tactile discs and the tactile cells, inasmuch as mitochondria from the former enter into the latter,[3] and in particular since the neurofibrils pass from the tactile discs into the tactile cells and there enter into a network. Between each two cells there lies the expansion of a nerve in the form of a tactile disc. The medullated nerve fiber enters the corpuscle from the side and loses its medulla; while the axis cylinder spreads out within the tactile corpuscle as a delicate, compact network of fibrils. At the same time the fibrillar sheath of the nerve fiber passes into a delicate connective-tissue sheath for the whole corpuscle. The number of tactile discs is naturally one less than the number of tactile cells. Even though two or more tactile discs may be present, only a single nerve fiber enters into the corpuscle.

In contrast to the simple tactile cells, the corpuscles of Grandry are not found in epithelium but only in connective tissue; and chiefly in the beak and tongue of many birds (water-fowl). They do not occur in mammals or in man.

The corpuscles of Meissner or Wagner form the second group of **tactile corpuscles.** Pl. 36, Fig. 2 They are elongated, ellipsoidal bodies, 60—150 μ long and 30—60 μ broad, and have a Pl. 88, Fig. 3 distinctly striated appearance. They are exceedingly numerous in man and are found in large numbers in the papillae of the corium, particularly in the palm of the hand and in the sole of the foot. They consist of flat tactile cells lying one upon another, the nuclei of which are also flattened. Between them are found the terminal fibrillar expansions of the axis cylinders of the nerve fibers, two to five in number, which enter the lower pole of the corpuscle;[1] although occasionally a nerve fiber enters the side of the corpuscle having previously lost its medulla. Each tactile corpuscle is surrounded by a connective-tissue sheath which commonly produces superficial constrictions of the corpuscle.

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[1] As regards the occurrence of tactile cells, they are rather infrequent in man, noticeably so in the epidermis where in other animals they are constantly found. They are particularly abundant in the epidermis in the snout of the pig. They are also common in the hard palate and in the external root sheath of the tactile hairs of many mammals. When they occur in the corium it is probable that they are epithelial cells which have been moved from their original place. Recently they have been described from the corium of the sole of the foot as being surrounded by the coils and loops of a nerve termination.

[2] The breadth of the cell is the same as that of the entire corpuscle, 50 μ.

[3] A similar connection of the chondriome is said to obtain between the tactile cells and the cells of the capsule.

2. End Bulbs (Lamellar Corpuscles)

The essential characteristic of an end bulb is that the entire or subdivided termination of the axis cylinder of a medullated nerve fiber shall be surrounded by a so-called internal club composed of a quantity of neuroplasm which usually is not very great. The club thus constituted is surrounded by more or less voluminous sheaths of connective tissue. In this category belong chiefly the simple end bulbs of the conjunctive, the genital corpuscles and the **lamellar corpuscles.** Since the latter are the most elaborately developed end bulbs they will be described first. Two varieties of lamellar corpuscles are known, the smaller CORPUSCLES OF HERBST from the beaks and tongues of water-fowl, and the VATER-PACINIAN CORPUSCLES of mammals and man (corpuscula lamellosa). The latter are large and ellipsoidal, 0.5—1.5 mm. long and about half as broad, easily visible to the unaided eye and distinguished by numerous nucleated sheaths of connective tissue arranged in lamellae. A zone of delicate lamellae lying close around the inner bulb is to be distinguished from a broader external zone of wider lamellae. The number of lamellae varies with the size of the corpuscle and may be as much as 50 or more. Each lamella consists of delicate connective-tissue fibers running longitudinally and transversely and of flat endothelium-like connective-tissue cells. The external lamellae contain also fine elastic fibers. Between each two lamellae there lies a small quantity of fluid.

Pl. 37, Figs. 4, 6

The slender INNER BULB of the Vater-Pacinian corpuscle is finely granular and contains no nuclei. Within it runs the axis cylinder, whose fibrillar connective-tissue sheath blends with the lamellae; while the medullary sheath continues through the lamellae but ceases at the beginning of the inner bulb. The relatively thick axis cylinder forms the axis of the inner bulb, terminating at its opposite end by dividing or by becoming slightly swollen. According to the results of recent methods of investigation the axis cylinder appears to fill the whole inner bulb with its network of fibrils. In addition to the chief nerve fiber there is present a second axis cylinder with very delicate independent branches. The larger corpuscles show also blood capillaries between the lamellae.

The CORPUSCLES OF HERBST are distinguished from the larger Vater-Pacinian corpuscles not only by their lesser size (140 μ long; 80 μ broad) but by the fact that their lamellae are much less numerous. Their inner, narrow lamellae contain no nuclei. On the other hand the inner bulb bears externally a single row of nuclei which probably belong to the sheath of Schwann.

Pl. 37, Fig. 5

Vater-Pacinian corpuscles are widely distributed in the human body. They are found chiefly in the subcutaneous adipose tissue of the palm of the hand and of the sole of the foot, in the neighborhood of joints, in the periosteum, in many tendons and fasciae, and in many localities within the peritoneal cavity, *e. g.* in the pancreas and in the mesentery. Very large and numerous corpuscles are found in the mesentery of the cat.

A SIMPLE, cylindrical END BULB, as found in the conjunctiva and in many mucous membranes, consists of axis cylinder and inner bulb surrounded by a weak connective-tissue sheath formed from the fibrillar sheath of the medullated nerve fiber. There are also spherical end bulbs of similar structure.

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[1] In addition to the expansions of the chief nerve fiber or fibers of the corpuscle there may be observed the expansion of another fiber which is independent of the first group.

Occupying a place between the lamellar corpuscles and the simple cylindrical end bulbs are the GENITAL CORPUSCLES. In these the inner bulb is surrounded by several distinct sheaths, but the behavior of the axis cylinders is somewhat unusual. They enter the bulbs at various places and subdivide within them, forming a much coiled plexus. Here belong also the Golgi-Mazzoni corpuscles found in the plantar pads of the cat.

V. The Organs of Digestion

The organs of digestion consist of a tube, the digestive tract, beginning at the mouth and ending at the anus; and of the related glands, some of which lie in the wall of the tube itself while others — the larger glands, salivary glands, pancreas and liver — merely penetrate the walls with their excretory ducts. The digestive tract (and other tracts lined by mucous membrane are similar)[1] consists of the following layers:

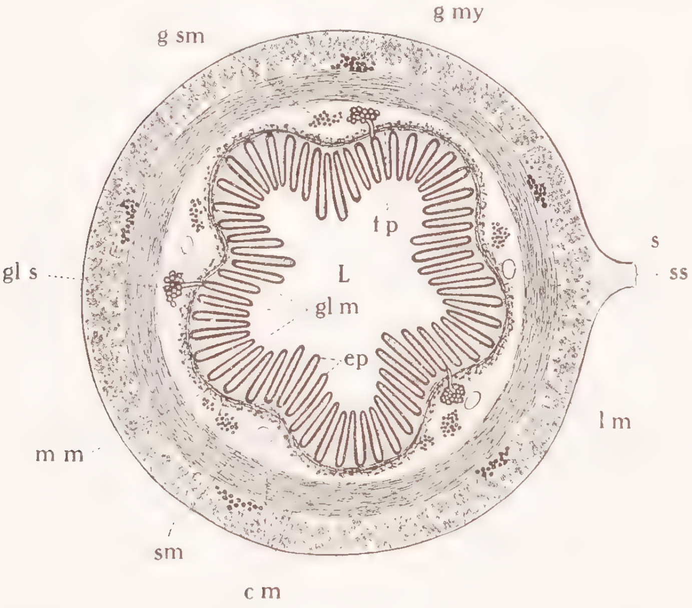

Fig. 23. **Diagram of the Structure of the Wall of the Digestive Tract.**

c m	circular muscle
ep	epithelium
g my	ganglion of plexus myentericus
g sm	ganglion of plexus submucosus
gl m	glands of mucous coat
gl s	glands of submucosa
L	lumen
l m	longitudinal muscle
m m	muscularis mucosae
s	serosa
sm	submucosa
ss	subserosa
t p	tunica propria

Fig. 23 a. The MUCOUS COAT proper, *tunica mucosa*. This in turn is composed of 1. *epithelium*; 2. *tunica propria*, which may contain straight or branched tubular glands, excretory ducts of glands lying in the tunica submucosa and solitary lymph nodules; 3. the *lamina muscularis mucosae*, a layer (occasionally subdivided) of smooth muscle. These three portions of the mucous coat are closely connected and share equally in forming the folds of the mucous coat.

b. The *tunica submucosa*. This lies beneath the mucous coat and is formed essentially of loose connective tissue. It contains the larger vessels and nerve trunks for the mucous coat, and frequently glands (branched tubular or tubulo-alveolar), solitary and aggregated lymph nodules, frequently also adipose tissue. The loose character of the tissue renders possible the formation of folds of the mucous coat upon the substratum.

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[1] The respiratory tract, genito-urinary tract, etc. These never have the tunica muscularis mucosae, but a tunica submucosa is always indicated more or less clearly.

c. The MUSCULAR COAT, *tunica muscularis*, lies external to the tunica submucosa and usually consists of smooth muscle which is commonly subdivided into inner circular and outer longitudinal layers. Between the two layers the nerve supply of the muscle forms a gangliated plexus named the *plexus myentericus* (of AUERBACH), in contrast to the similar plexus of the nerves of the mucous coat, which lying in the tunica submucosa is known as the *plexus submucosus* (of MEISSNER).

d. The muscular coat is commonly covered by the *tunica serosa*, the outer surface of which bears the serous epithelium. Frequently beneath the serosa is a layer of loose connective tissue, the *tunica subserosa*, which occasionally contains adipose tissue.

Of these layers the mucous coat is constantly present in the digestive tract; any of the others, and even the lamina muscularis mucosae, may occasionally be lacking. In the stomach, small intestine and large intestine all the layers are to be found. The presence of the serous covering depends upon the situation of the organ in question within the body cavity.

1. The Oral Cavity

The mucous coat of the oral cavity has throughout a stratified squamous epithelium with papillae (p. 35). The latter in some areas are very long and extend deep into the epithelium (as much as ½ mm) as in the GUMS *(gingiva)* and MARGINS OF THE LIPS. The mucous coat consists of connective-tissue bundles and numerous elastic fibers.

The tunica submucosa in certain areas is formed of dense and firm connective tissue which is fused with the layer beneath, *e. g.* the periosteum of the palate; for the mucous membrane of the hard palate is not moveable upon its substratum. A tunica muscularis mucosae is not present in any part of the oral cavity. The tunica submucosa, so far as it is present (see above), contains many glands of tubulo-alveolar form. Their size varies from that of a millet seed to that of a pea. In structure they are similar to the large salivary glands (p. 193).[1]

The BLOOD VESSELS of the oral mucous membrane form a coarse submucous plexus; while within the mucous coat there lies a finer plexus from which capillary loops extend into the papillae. The lymphatic vessels have a similar course. The NERVES also form a submucous plexus and terminate partly in free endings within the epithelium and partly within corpuscles.

a. The Lips and Cheeks

On their anterior surfaces the **lips** have a covering of skin which shows all its usual characteristics (p. 296). At the margin of the lip the skin passes into a region where the papillae are very long; and this in turn passes gradually into the oral mucous membrane Pl. 41, Fig. 3 of the posterior surface of the lip, the papillae of which are much lower. In all this course the hairs are first lost, then the sebaceous glands, which are to be observed for a short distance on the margin of the lip beyond the hairs. Their number is highly variable and occasionally they are entirely lacking. The epidermis loses its highly developed stratum granulosum and passes into the stratified squamous epithelium of the oral cavity in such fashion that the stratum germinativum is continued into the deeper layers; while the stratum corneum is continuous with the flattened cells of the superficial layers. Beneath the skin lies the muscle of the lip, consisting of the striated fibers of the musculus orbicularis oris in compact bundles, and in front of them the less compact bundles of the remaining musculature of the lip. Between muscle and mucous membrane the glands of the lips, glandulae labiales, lie in a kind of submucous layer (for details see p. 198). They vary in size from a millet seed to a pea and always lie above the greatest convexity of the lips. In the lower lip their number is somewhat greater than in the upper lip.

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[1] As to the distribution of these glands within the oral cavity see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II.

The **cheeks** are extremely like the lips in structure. The most important difference between the two being that the cheeks are by far the richer in elastic tissue. This tissue consists of firm masses of coiled fibers and forms a dense layer which lies at a slight depth beneath the epidermis and is interrupted by the hairs of the cheek. The glands of the cheeks, particularly the middle and posterior glands, lie either within the substance of the buccinator muscle, or even on its external surface. Only the anterior glands of the cheek which immediately adjoin those of the lip lie, like the latter, in the submucosa. In general, glands are not so abundant in the cheeks as in the lips.

b. The Teeth

The **teeth** are hard structures formed by the oral mucous membrane[1] and show in
Pls. 38, 39 their interior a narrow cavity, the pulp cavity, *cavum dentis*, open at the apex of the root. In the living tooth the pulp cavity contains a soft mass of tissue, the **tooth pulp,** *pulpa dentis*, formed of connective tissue containing numerous cells and relatively few fibers. In many ways the pulp of the tooth shows the characteristics of embryonic or gelatinous connective tissue (p. 62). Thus it contains numerous fine fibers that are not arranged in bundles. The nerves and vessels of the tooth lie chiefly within the pulp. In addition to
Pl. 39, Fig. 3 rounded and stellate cells the pulp tissue shows on its surface a single layer of cells arranged
Pl. 39, Fig. 4 like those of an epithelium, and closely related to the osteoblasts of bone. In this situation the cells are termed ODONTOBLASTS. They have an elongated, almost low-columnar form, often with a rounded end turned toward the pulp cavity. The nucleus lies in this end, while from the opposite pole of the cell there proceeds the DENTINAL FIBER which extends into the dentine. This relation is especially clear in young individuals in whom a connection of the odontoblasts with the remaining cells (usually branched) of the pulp is distinct.

The hard substance of the tooth is formed of three materials of which one, the ENAMEL, is of epithelial origin; while the other two, the DENTINE which forms the chief mass of the tooth, and the CEMENT, are derived from connective tissue. Enamel and dentine are characteristic of teeth and occur nowhere else. On the other hand the cement is osseous tissue. In the three portions of the tooth which may be distinguished macroscopically, crown, neck and root, the three materials are distributed in such fashion that the dentine, which is present in both crown and root, never reaches the surface of the tooth but surrounds the pulp cavity. It thus forms the inner layer of the wall of the tooth. In the region of the crown, the enamel covers in the dentine like a cap, but becomes thinner towards the neck, where the cement begins as a thin layer which grows thicker towards the root. In the crown of the tooth the dentine is thus covered by enamel and in the neck by a thin layer of cement which becomes a thick layer in the root.

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[1] The teeth are strictly formations of the skin and ectoderm, not of the endoderm; since the part of the mouth in which they are formed, the stomadeum, is not by origin part of the endodermal tract. In accordance with the foregoing certain lower vertebrates have teeth in the skin also.

The **dentine, substantia eburnea,** is a modified bone tissue, but harder than bone, and consists of a calcified matrix and uncalcified fibrils. It is penetrated by fine canals, Pl. 38, Figs. 1-3, 5 the dentinal tubules, which begin at, and radiate from, the pulp cavity. The principal Pl. 39, Figs. 1—3 difference between dentine and bone is that the dentine itself contains neither cells nor vessels. In the dentinal tubules there are to be found only processes of the odontoblasts, the DENTINAL FIBERS (see above).

As regards the finer structure of the dentine the fibrils of the calcified matrix are arranged chiefly in the long axis of the tooth; although in the crown they lie almost parallel to the grinding surface. In addition the curvature of the dentinal canals, to which the fibers run at right angles, has an influence upon the direction of the latter. The dentinal canals or tubules are slender canals whose diameter, near their opening into the pulp cavity, may be as much as 4 μ. Towards the external surface of the dentine (that is toward the enamel-dentine or the cement-dentine contact) they divide several times at acute angles; and finally, having given off many delicate lateral branches and at the same time having constantly diminished in diameter, they terminate at the very boundary of the dentine in delicate blind-ending branches about 0.5 μ in diameter. Their course is not straight but is slightly curved, and often, as in the neck and root of the tooth, is sinuous like a much elongated letter S.[1] The lateral branches afford connections with neighboring canals, although the blind ends rarely anastomose. The canals contain the so-called DENTINAL FIBERS which are processes of the osteoblasts. Apart from a more or less straight course in the crown of the tooth the behavior of the dentinal tubules is somewhat different in different regions of the tooth. In the first place the lateral branches increase considerably in number as the diameter of the tubule diminishes towards the enamel or the cement. In the crown the delicate ends of the tubules often extend into the enamel; while in the neck and in the root they extend at the most as far as Tomes' granules (see below). The dentinal tubules, like the lacunae and canaliculi of bone (p. 79) are surrounded by a sheath of their own which bears the name of NEUMANN'S SHEATH. Since they are not dissolved by boiling they do not consist of collagen. In addition they are resistant to acids and alkalis.

In the dentine of the crown of the tooth, not far from its line of contact with the enamel, there are to be seen in a GROUND SECTION of tooth, angular cavities of irregular form, the surface of which is made up of segments of smaller spheres. These spaces, termed INTERGLOBULAR SPACES, are probably occupied by remnants of uncalcified dent- Pl. 38, Fig. 2 ine and in different individuals are highly variable both in number and in size. The small Pl. 39, Figs. 1, 2 masses of calcified dentine, parts of whose surfaces form the boundaries of the spaces, are known as dentinal spherules. Similar, but much smaller, spaces are constantly found at the dentine-cement contact, but for the most part external to the ends of the dentinal tubules. Here they form a continuous boundary layer, the so-called TOMES' GRANULAR LAYER, between the dentine, which is penetrated by canals, and the cement.

The **enamel, substantia adamantina,** consists of long, somewhat irregular, hexagonal prisms, the ENAMEL PRISMS OR ENAMEL FIBERS, 3—6 μ wide, which traverse the entire Pl. 38, Figs. 1—4 thickness of the enamel and are united by a small quantity of cement. Both cement and Pl. 39, Fig. 1 prisms are calcified. The surfaces bounding the prism are usually not flat on all sides, certain of them being concave or, as it were, grooved. The enamel prisms do not run a straight course from the dentine to the surface of the tooth, but show a more or less distinctly spiral bending. In places they even form a whorl. The enamel prisms are structureless. They represent the hardest tissue of the body and contain practically no organic material (2—3%).[1] Consequently they dissolve almost completely in mineral acids. Occasionally after the action of certain reagents they appear transversely striated (see below). They are negatively doubly refractive. Since the enamel prisms run through the entire thickness of the enamel they must be thicker at their outer ends than at their ends next to the dentine.

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[1] The curvature of the dentinal canals shows a certain regularity, inasmuch as the convexity of the first bend is towards the root, and of the second towards the crown. In addition to these two chief curvatures there are secondary curves in the neck and root.

The course of the enamel prisms is very complicated. In the first place an arrangement in groups may be recognized. About twenty prisms form a group and run in the same direction, which crosses that of neighboring prism groups. Only in the neighborhood of the dentine and near the surface of the enamel do the enamel prisms have a rather strictly radial course. In between these limits there are extensive lateral curvatures which are more marked in the middle fibers of a group than in the marginal fibers, and which may amount even to spiral courses. The appearance of the so-called enamel lines of SCHREGER depends upon this peculiarity in the course of the enamel prisms. These lines are seen as alternately light and dark radial striae when a ground section of tooth is illuminated obliquely by reflected light.

Pl. 38, Fig. 3

The so-called parallel lines of RETZIUS are always to be recognized in ground sections of tooth. They depend upon the deposition of the enamel in layers and show a more or less distinctly brownish colour. Their origin at the surface is in fine furrows between the so-called enamel ridges of the tooth, *i. e.* between delicate, girdlelike thickenings of the surface of the enamel, which are demonstrable only in the permanent teeth.

Pl. 38, Fig. 2

Interruptions occur in the process of the calcification of the enamel; the shorter interruptions producing transverse lines which appear quite distinctly after certain methods of treating the enamel lightly with acid. The longer interruptions in the process have as their result the lines of RETZIUS described above.

So-called tufts of enamel fibers extend outward from the surface of the dentine, adapting themselves to the curved courses of the enamel prisms and radiating between them towards the surface. They extend more or less deeply into the enamel and consist of masses of the uncalcified cement substance of the enamel itself. They have nothing whatever to do with the dentine and its canals.

The surface of the enamel is covered by a structureless membrane, the **enamel membrane, cuticula dentis.** It is only 1—2 μ thick, but is very resistant to reagents.

Pl. 38, Figs. 1, 5
Pl. 39, Figs. 2, 5

The **cement, substantia ossea,** is simply ordinary bone tissue, but without the structure of bone; *i. e.* without blood vessels or Haversian canals and usually without lamellae; and where it is thinnest, at the neck and upper part of the root of the tooth, it is even without bone corpuscles. Only the very largest teeth such as those of the larger mammals have lamellae in the cement. In these cases Haversian canals are frequently found. In man, even lamellae are very rare, occurring only in old molar teeth.

The enamel represents a completely dead, almost purely inorganic substance which in fully developed teeth no longer shows any of the phenomena of life; in particular it is no longer capable of growth. Young enamel, to a slight extent, shows a certain growth by intussusception; but later every possibility of further growth and of the replacement of lost enamel ceases. On the other hand the dentine shows not merely change of substance, but there is the possibility of replacing lost dentine by the so-called secondary dentine, such as occurs when dentine is extensively worn away through mastication. Most important of all, dentine appears to grow continuously. Thus it may be shown that the diameter of the dentinal tubules constantly diminishes with age.

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[1] Results vary as to the inorganic content of enamel. While, for a time, the inorganic material was considered to constitute even 100%, it is the more recent opinion that enamel contains as much as 4—5% of organic material.

The blood vessels, lymphatic vessels and nerves[1] of a tooth lie only in the pulp; the dentine is completely free from them and naturally enamel is the same. The cement also, as a rule, contains no blood vessels.

Appendix: The Development of the Teeth

Even more than in the case of the development of bone the structure of the completed tooth reflects perfectly the course of its development. The main facts of the development of a tooth will now be briefly reviewed. Pl. 40 Pl. 41, Figs. 1, 2

The teeth, in the manner of their development, are products of the oral mucous membrane (p. 184) being formed partly by the epithelium and partly by the connective tissue of the mucous membrane. Figs. 24, 25 The development is initiated by the epithelium which projects into the connective tissue beneath it in the form of a continuous ledge parallel to the border of the jaw, but it does not at first give evidence of the anlagen of the individual teeth. This so-called **enamel (or dental) ledge** appears in man towards the end of the second month of embryonic life, accompanied by a further ingrowth of epithelium which marks off the lips and cheeks from the margin of the jaw.

Soon after, at certain points corresponding in number and position to the later deciduous teeth, there are found knoblike swellings on the epithelium of the dental ledge, the anlagen of the so-called **enamel organs.** These are situated immediately above the free border of the ledge, and on its labial or buccal side. At the same time there appears in contact with each enamel organ a condensation of connective-tissue cells, the anlage of the **dental papilla.** The young enamel organ becomes flattened where it is in contact with the papilla, and the flattening soon becomes an invagination; so that the enamel organ rests like a cap upon the anlage of the papilla.

Through a simultaneous enlargement of enamel organ and papilla the former maintains its position like a cap upon the latter, and at last the anlage of each individual tooth Pl. 40, Fig. 3 becomes constricted from the common dental ledge; as a result, after a certain period of development the anlage of the tooth is connected with the dental ledge only by a lateral strand of ectoderm.

After the anlage of the deciduous tooth is provided for by enamel organ and dental papilla, the anlage of the **permanent tooth** develops at the free (lower) border of the dental ledge by a very slow and very gradual repetition of the above process.

While retaining its caplike form the enamel organ soon shows a differentiation of its elements. Its outer surface is formed at first of low columnar cells which surround the more loosely arranged cells of the interior. At the summit of the invagination caused by the young papilla, the columnar cells, which are also invaginated at this point, form an Fig. 24 irregular mass of closely packed cells, the so-called **enamel knot.** A cord of closely arranged cells, the ENAMEL CORD, connects the cells of the enamel knot[1] with the neck of the enamel organ, *i. e.* with the point of union between the enamel organ and the epithelium of the dental ledge.

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[1] Up to the present nerves have not been successfully demonstrated in dentine. It is highly improbable that true nerve fibers or nerve terminations can be demonstrated in dentine. The transmission of sensations of pain occurs through the dentinal fibers of the odontoblasts, between the bodies of which the nerves of the pulp terminate in knoblike thickenings.

The initiative in the formation of a tooth lies with the oral epithelium, that is to say, with the enamel organ described above; the connective tissue papilla plays a purely passive role. Thus the enamel organ enlarges actively by expansion at its surface, a process which causes the embryonic connective tissue of the papilla to become compressed.

In its further growth the form of the enamel organ changes from that of a flat cap Pl. 40, Fig. 3 into that of a bell, during which process the papilla assumes the form of the crown of the developing tooth. Thus in a certain sense the enamel organ determines the form of the crown of the tooth. The entire process of tooth formation in the embryo supplies only the crown of the tooth, the root not being formed until much later. The dental papilla becomes constantly more cellular and vascular and completely fills the cavity of the bell. It consists of embryonic connective tissue and shows on its surface immediately in contact with the enamel organ, a layer of connective-tissue cells arranged like an epithelium. The cells of this layer, because of their activity in forming the dentine, bear the name of ODONTOBLASTS.

THE bell-shaped ENAMEL ORGAN during its growth SINKS MORE AND MORE DEEPLY INTO THE TISSUES OF THE JAW and as it expands it extends more and more into the lower layers of the mucous membrane. As it thus moves away from the dental ledge the marked Pl. 40, Figs. 3. 4 differentiation of its epithelial cells may be recognized. The innermost layer of cells, *i. e.* those which have been invaginated by the papilla and rest directly upon it, are high columnar in form and show a very regular arrangement. Because these cells alone form the enamel they are named **adamantoblasts** or ameloblasts. The outer cells of the bell-like enamel organ, *i. e.* those which bound this organ towards the surrounding ordinary connective tissue, are flat-cubical and are called OUTER ENAMEL CELLS. Almost the entire remaining space within the enamel organ is occupied by cells which have undergone a remarkable transformation such as never occurs to epithelial cells elsewhere. The cells have become star-shaped and are connected with one another by processes just as are connective-tissue cells, which they resemble to an extraordinary degree; moreover a soft mucous intercellular substance has developed between them. This mass of tissue within the enamel organ is termed the ENAMEL PULP. Only the cells which lie immediately next to the adamantoblasts in a narrow compact zone (so-called intermediate layer) retain their original form. In addition a strand, formed also of compactly arranged cells, the ENAMEL CORD which developed from the earlier enamel knot, comes now much more distinctly into evidence. It traverses the enamel pulp, joining the apex of the papilla, or rather the adamantoblasts which lie upon it, with the outer enamel cells.[2] As the tension upon it increases this epithelial cord becomes thinner and thinner and soon disappears altogether (see below). The free end of the dental ledge remains unaltered on the lingual side of the enamel organ and does not participate in the developmental processes described above. There arises from it the anlage of the permanent tooth which is soon recognizable. This stage of development is reached by the deciduous tooth in the fourth month of embryonic life; no hard substance has as yet been formed.

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[1] The enamel knot is bounded on all sides, labial as well as dental, by a shallow furrow, the so-called ENAMEL FURROW.

[2] In the anlagen of many teeth, but not of all (*e. g.* not in those of the temporary incisors or the permanent molars), there exists at the point where the enamel cord fuses with the outer enamel cells a depression in the surface of the organ, the so-called ENAMEL UMBILICUS.

The enamel organ steadily enlarges and the bulk of the enamel pulp increases and lies chiefly at the sides of the anlage proper (*i. e.* around the papilla and layer of adamantoblasts) which presses more and more deeply into the mass of enamel pulp. Before the formation of the hard substances takes place the anlage of the permanent tooth may be observed at the free border of the dental ledge on the lingual side of the deciduous tooth, in the form of a young caplike enamel organ surmounting a young papilla. The first hard substances appear at the end of the fifth, or at the beginning of the sixth embryonic month, at the apex of the dental papilla,[1] where the first dentine is formed; the formation of the enamel soon follows. The dentine is formed by the **odontoblasts**[2] which play the same part in the formation of dentine as do the osteoblasts in forming the related bone tissue. Since the formation of dentine is first noticeable at the apex and thence gradually extends down the sides of the papilla, the heaviest layer of dentine is always found covering the apex.

Pl. 40, Fig. 4
Fig. 25

Since the dentine differs in many respects from the nearly related bone tissue, especially in not containing cells, its formation proceeds in a somewhat different manner. Before the deposition of salts of calcium begins there may be recognized a delicate, uncalcified, membrane-like layer, appropriately named the membrana preformativa, consisting of so-called PREDENTINE, and intervening between the adamantoblasts and the odontoblasts. It appears structureless but is continued as a superficial layer of radial fibers, so-called fibers of Korff, which pass between the odontoblasts and blend with the connective-tissue fibers of the papilla. At the same time the odontoblasts send out processes, the so-called Tomes' fibers, into the layer of young dentine; these with their end knobs extend even between the adamantoblasts. The deposition of salts of calcium begins in that part of the young dentine which lies farthest from the surface of the papilla; as a result there is always demonstrable a layer of uncalcified predentine immediately bordering the odontoblasts. At the same time the permanent, tangential fibers of the dentine develop (p. 185) while the radial fibers of the predentine seem to be altogether used up in forming the dentine.

Somewhat later than the appearance of the dentine, but always before calcification begins, the first **enamel** is formed by the **ameloblasts.** These cells have now assumed a high columnar form; their nuclei have retired to the ends most distant from the papilla. The height of the cells during the formation of the enamel is considerable (100 μ); towards the region of the future neck of the tooth their height diminishes. As is the case with the osteoblasts, there is but little increase in the number of cells by mitosis. A narrow homogeneous zone is next formed on the surface of the whole layer of cells; then each cell sends out toward the young layer of dentine a prismatic process of a form corresponding to its own, the so-called TOMES' process. These processes are united by cement, just as are ordinary columnar cells; however the cement, at least at first, is strikingly abundant. Neither the cement substance nor the Tomes' processes are at first calcified. The Tomes'

Pl. 40, Fig. 4
Fig. 25

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[1] If the anlage is that of a multituberculate tooth the papilla shows several apices upon each of which the same process occurs.

[2] The odontoblasts, which no longer increase by mitosis after the transformation of the fibers of Korff (see above), are pressed close together and in places form a double row.

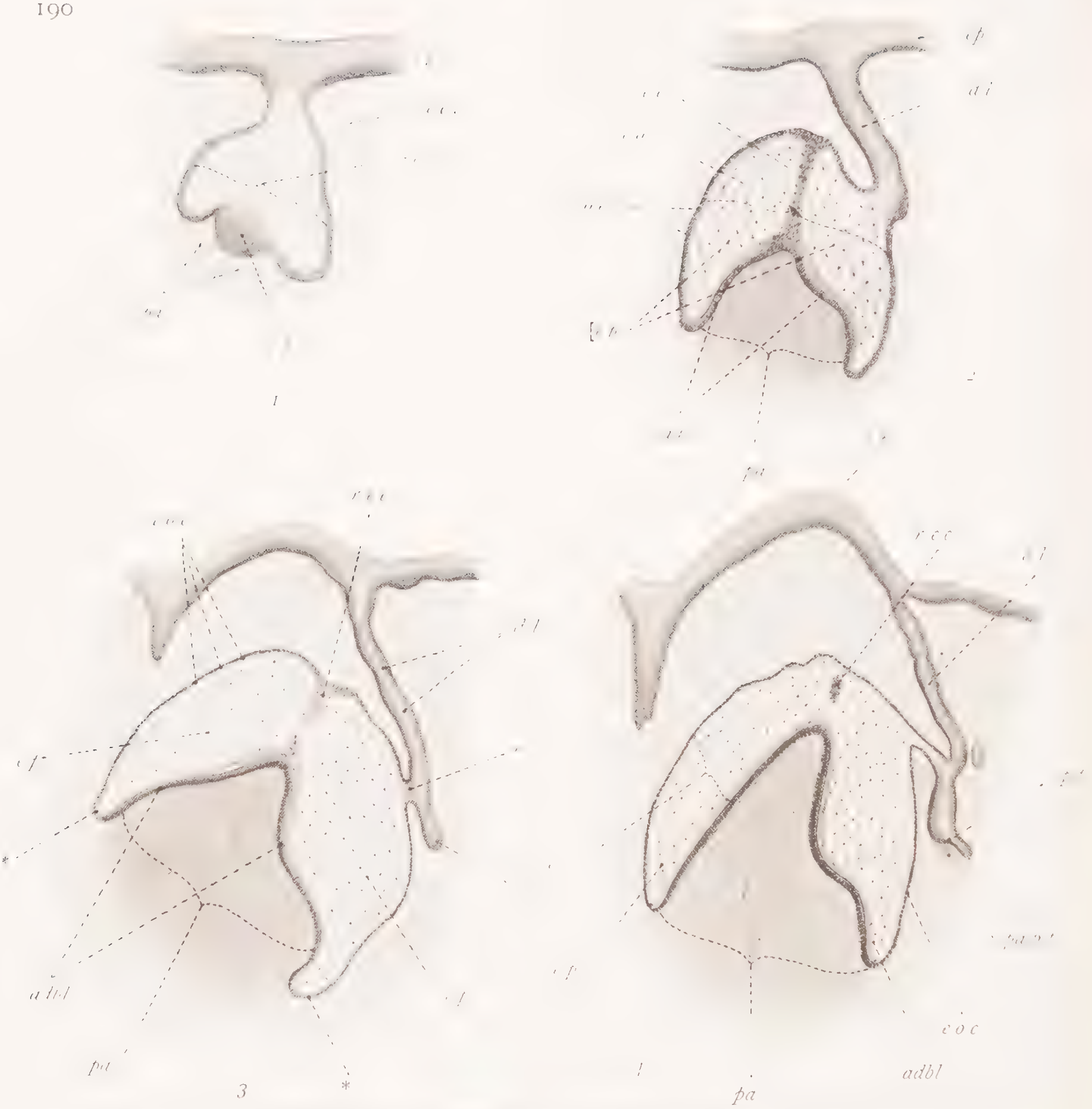

Fig. 24. **Four Diagrams of the Embryonic Development of a Tooth Previous to the Appearance of the Hard Substances.**

1 = Early stage of enamel organ with enamel knot.
2 = Further development of the anlage of the tooth; caplike enamel organ with enamel cord; papilla.
3 = The margins of the enamel organ are growing around the papilla; early anlage of permanent tooth; neck of enamel organ.
4 = Shortly before the appearance of the hard substances; distinct anlage of the permanent tooth.

adbl = adamantoblasts
d l = dental ledge
e c = enamel cord
e c t = embryonic connective tissue
e k = enamel knot
e o = enamel organ
e p = enamel pulp
ep = oral epithelium
n = neck of enamel organ
e o c = outer enamel cells
pa = papilla
(pa) = anlage of papilla
pa p t = papilla of permanent tooth
p t = anlage of permanent tooth
r e c = remains of enamel cord
+ = free border of dental ledge
* = margins of enamel organ

processes are usually regarded as secretion products of the adamantoblasts.[1] With the progressive elongation of the processes calcification also begins and extends within the processes, but not within the cement. Since the adamantoblasts which lie above the apex of the papilla are the first to form cement, the processes or young enamel prisms are longest in this region; just as the young layer of dentine has its greatest thickness in the same locality.

While the formation of the hard substances is making itself evident in the embryonic tooth, the latter has reached a proportionately large size and has lost its connection with the dental ledge and with the oral epithelium. The neck of the enamel organ, which does not share in the rapid growth of the tooth, is broken by inroads of the connective tissue and as a rule finally disappears. A similar fate overtakes the dental ledge itself although remnants, the so-called glandulae tartaricae, are occasionally found as epithelial pearls in the gums.

The further development of hard substances proceeds in the embryonic tooth essentially as above described. However not only does a continual elongation of the enamel prisms take place, but also a decided increase in their diameter at the expense of the cement which constantly diminishes in amount and at last becomes calcified. With the growth of the embryonic tooth, which as previously related consists at first of the dental papilla and the layer of adamantoblasts, the bulk of the enamel pulp grows constantly less. The enamel pulp serves, so to speak, to reserve a place for the growing tooth.

The enamel pulp and the outer enamel cells disappear completely. The enamel cuticle is formed by the inner enamel cells when the production of enamel ceases, and appears as a membrane lying on that surface of the adamantoblasts which was engaged in forming enamel.[2]

The epithelial connection of the dental ledge which exists between the anlage of the deciduous tooth and that of the permanent tooth disappears entirely with the obliteration of the dental ledge. It follows from the mode of formation of the crown of the tooth described above that the papilla becomes relatively smaller and smaller. It gives rise at last to the dental pulp of the fully developed tooth.

The process as above described serves to effect the gradual formation of the CROWN OF THE TOOTH ONLY. The formation of the root of the tooth does not occur before birth but at the time of the eruption of the teeth. *Fig. 1, Pl. 41* shows well the extent to which the formation of the deciduous and permanent teeth have advanced at the time of birth. The FORMATION OF THE ROOT occurs shortly before the eruption of the tooth: the process involves also the formation of the neck of the tooth, which histologically is not to be separated from the root. It proceeds first by the elongation of the papilla in a direction opposite to its apex; and also by the elongation of the margin of the enamel organ, where the inner and outer epithelial cells are continuous and consist merely of two single layers of epithelial cells separating the dense connective tissue from that which lies externally.[1] Neck and root thus slowly form, joined to the anlage of the crown. The development of hard substances proceeds steadily, and in neck and root continues after the eruption of the tooth (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II). The formation of the dentine of the root now proceeds exactly in the same way as did the formation of the dentine of the crown during embryonic life, the bulk of the pulp tissue diminishing

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[1] Recent views on the formation of enamel differ considerably from the above. The view is now advanced that the enamel prisms are not projections secreted by the adamantoblasts, but that the entire process of forming enamel proceeds in an INTRA-EPITHELIAL manner. Thus the adamantoblasts possess two cuticular layers, an inner between the prismatic processes and the bodies of the cells proper with their nuclei, and an outer which separates the enamel prisms from the young dentine layer and which, in fact, often constitutes a very distinct limiting membrane (Fig. 4, Pl. 40).

Consideration of the enamel of the teeth of lower vertebrates, which is formed quite differently, has recently given rise to the assertion that the enamel of mammals is nearly related to the dentine and does not fundamentally represent a truly epithelial formation; but in the widest sense of the words belongs to the dentine.

[2] According to this conception the layer of inner enamel cells, and consequently the whole enamel organ, disappears without leaving a trace.

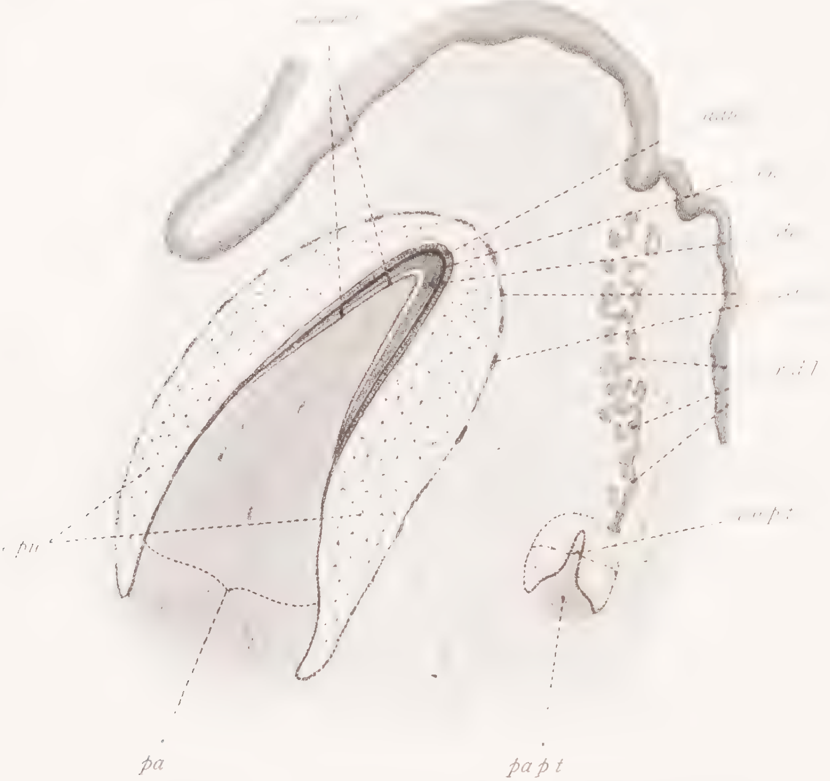

Fig. 25. **Diagram of the Development of a Tooth, Stage II.**

Stage of the appearance of the hard substances and of the enamel organ of the permanent tooth. The layer of odontoblasts has formed young dentine on the surface of the papilla. The layer of young enamel formed by the adamantoblasts lies immediately upon the dentine. The form of the crown of the later deciduous tooth is quite noticeable.

en = enamel
adbl = adamantoblasts
de = dentine
e o p t = enamel organ of permanent tooth
e pu = enamel pulp
odonbl = odontoblasts
pa = papilla
o e c = outer enamel cells
pa p t = papilla of permanent tooth
r d l = remains of dental ledge

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[1] Although the epithelium of the enamel organ has, in this situation, no functions to perform yet it initiates here the formation of the root. In this fact may be recognized its great formative power, and the relative or complete powerlessness of connective tissue in the same direction.

as the thickness of the wall of dentine increases. The FORMATION OF THE CEMENT now begins, and this being true bone tissue (p. 186) proceeds by the ossification of the connective-tissue dental sac. This is the name given to the sheath of fibrous connective tissue which may be observed in a relatively early embryonic stage immediately surrounding the anlage of the tooth. In the region of the crown the sac soon disappears through overdistention as the enamel organ elongates; but it continues to surround the root firmly, breaking through the enamel organ and finally causing its obliteration. As a result epithelial pearls, glandulae tartaricae, may be found in the cement. The bone substance arises in exactly the same way as in bone tissue elsewhere. As a consequence of the direct ossification of the connective tissue, the cement lies immediately upon the dentine of the root.

The development of the PERMANENT TEETH proceeds fundamentally in the same manner as does that of the deciduous teeth. It has already been mentioned that they arise from the free border of the dental ledge, that they lie on the lingual side of the deciduous teeth, and that at the time of birth they do not as yet contain any hard substance. The permanent molars are developed from a prolongation of the embryonic dental ledge which gives rise to the enamel organs of the individual molars in the same fashion as is described above for the deciduous teeth.

The loss of a deciduous tooth is accompanied by resorption of the entire root, including the neck and even parts of the crown. This is accomplished by the activity of osteoclasts. Thus only the crown, or at most only the crown and some remains of the neck are shed, and occasionally even parts of the crown have been resorbed.

With the progressive formation of dentine the soft, uncalcified, dental papilla becomes relatively smaller and smaller, and very soon the mass of the dentine is greater than that of the uncalcified tissue. When the formation of the dentine is completed, the uncalcified tissue of the papilla then remaining becomes the PULPA DENTIS.

In human teeth, corresponding to the small size of the cavum dentis, the amount of pulp tissue is also small; but in the teeth of many animals there is found proportionately a much larger pulp.

The formation of dentine ceases when the wall of the tooth attains its final thickness. However the odontoblasts retain their functional power and under certain circumstances dentine may again be formed, for example, if a tooth is damaged, as when the dentine of the wall has been much worn away through use. The dentine which may be formed in this manner is known as secondary dentine. It is distinguished from primary dentine by its peculiar dark, almost muddy, colour.

c. Glands of the Oral Cavity (Salivary Glands)

General

The following discussion of general structural features is based upon the large salivary glands and the smaller glands of the oral cavity, but also applies in large part to many small glands of the digestive, respiratory and urogenital tracts; also to the pancreas and to the lachrymal gland. These glands are, as a whole, of the exocrine type (p. 48). Some of them form a watery secretion which contains albumins (ALBUMINOUS OR SEROUS GLANDS), others a mucous secretion (MUCOUS GLANDS); in still others the secretion is a mixture of the preceding (MIXED GLANDS). The formation of secretion takes place in terminal secreting parts (p. 48), which form the chief part of the organ.

The cells of glands which form an albuminous secretion have a decidedly different appearance from those which secrete mucus, and the terminal parts which secrete mucus are somewhat different in structure from the contrasted variety which may be termed Pl. 44, Figs. 4, 6 **serous.** The latter are of small diameter, have a very small lumen which is often visible only with difficulty, and consist of cubical cells which in the fresh condition are dark by reason of the numerous granules which they contain. The nuclei of the cells are almost spherical and lie approximately in the middle of the cell. While the nucleus is somewhat nearer to the base of the cell than to its free surface it is never so close to the membrana propria nor so greatly flattened as it is in the cells of mucous glands. The boundaries between the serous cells, as a rule, are but little marked. The granular antecedents of the secretion are usually present as oxyphile granules, chiefly in the zone of the cell next to the lumen. In the stage when the cell is filled with secretion the granules form a dense mass; but when the cell has been emptied of secretion (exhausted) they are lacking. Many methods of preparation reveal a striation in the basal zone of the cell.

However many differences exist between the serous cells of individual glands. Thus Pl. 3. Fig. 8 when loaded with secretion the cells of the parotid gland, somewhat contrary to the above description, are filled with secretion to the base. The protoplasm in such a case appears honeycombed, the nucleus is compressed and often serrated, and the whole cell appears large. After the discharge of the secretion the cell becomes decidedly smaller, a striation appears in the basal zone and the nucleus again becomes spherical. (Intercellular secretion canaliculi (p. 45) are always to be found between serous cells even where their number is but few (*e. g.* in crescents, see below).

The terminal parts which secrete **mucus** are usually more tubular than alveolar in form and are of decidedly greater diameter (about twice as great). Their lumen is wide; under ordinary staining their cells appear clear, not granular (see under epithelial tissue); Pl. 44. Figs. 5. 6 usually their nuclei are markedly flattened against the base and are much serrated. When filled with mucus, and particularly shortly before its discharge which in the absence of secretory tubules takes place directly into the lumen, these cells are large, clear, vesicular structures. When empty they are much darker, but even then are very easily distinguished from serous cells because of their larger size and the position of the nucleus; for even after the discharge of secretion has taken place the nucleus lies close to the base of the cell. Secretion canaliculi are never found, but the boundaries of the cells are very distinct. There are terminal secreting parts which consist of mucous cells only (rare); others which contain only serous cells (more frequent), and still others in which both varieties are present (very common). This combination of the two varieties is always such that large areas of the epithelial wall of the secreting part consist of serous cells while the remaining portions, usually of considerable size, are formed of mucous cells. Usually in such mixed secreting parts the mucous cells so outnumber the serous cells that the latter are reduced to small groups which are applied like scales to the blind ends of the otherwise purely mucous secreting parts, and are known as crescents of GIANUZZI or EBNER (see below).

The external non-epithelial wall of the secreting parts of all salivary glands is formed by a basal membrane (membrana propria) which is apparently structureless but which, as is always the case with such membranes (p. 61), is composed of reticulum fibers. Usually the membrana propria of the larger mucous secreting parts is thicker than that of the parts which yield a serous secretion.

Invariably between the membrana propria and the secreting cells proper there are to be found extremely flat and strongly branched cells, which are of almost negligible

thickness except at the points where a nucleus, also flattened, is present. These cells, owing to their shape, have received the name BASKET CELLS. They are abundant and are Fig. 9
easily found in mucous glands but usually are somewhat infrequent in serous glands. Pl. 44, Fig. 5

It has already been related (p. 51, cf. also Fig. 9), that the basket cells are to be considered as myo-epithelial cells.

The purely serous glands of the oral cavity are the parotid gland and the so-called Ebner's glands in the region of the circumvallate papillae and of the papillae foliatae of the tongue. Purely mucous glands are rare; some are found in the palate (p. 203), at the base and borders of the tongue; and one portion or the other of the glandula sublingualis minor is often almost purely mucous. All the remaining glands, large as well as small, are mixed glands, in man the larger being the submaxillary glands, the glandulae sublinguales majores, and parts of the glandulae sublinguales minores. However there are differences, inasmuch as by far the larger portion of the human submaxillary gland contains purely serous parts which are lacking in the sublingual gland (see below).

In addition to the true crescents, that is to say, the small groups of serous cells, which in sections appear concave like a cap, other and different forms of crescents have been described; *e. g.* the so-called CRESCENTS OF EXHAUSTION, groups of mucous cells, which have been completely emptied of secretion.

The System of Excretory Ducts

In general the formation of secretion in salivary glands takes place only within their terminal parts (for exceptions see below), from the lumina of which the secretion pours into the delicate ultimate branches of the excretory duct. The latter, especially in the large glands, is very highly branched; indeed the number of secreting parts in the larger salivary glands is enormous. In the larger salivary glands the three following portions of the duct system may be distinguished; 1. the INTERMEDIATE (intercalated) DUCT (also aptly, but infrequently, termed the isthmus); 2. the SECRETORY OR SALIVARY DUCT (striated part); 3. the IMMEDIATE BRANCHES of the excretory duct proper. Each of these three divisions can be distinguished by its structure.

The **intermediate ducts,** as present in the human parotid and submaxillary glands and
in the pancreas, are the beginnings of the system of excretory ducts. Beginning where Pl. 45, Figs. 2, 4
the secreting parts end they collect the secretion from the latter. They are thin cylindrical Pl 53, Fig. 6
tubes of small diameter, but often of considerable length. The narrowest usually measure less than 12 μ across, while the lumen is remarkably small. Since they may unite with one another before emptying into the succeeding part of the duct system there may arise larger intermediate ducts which, however, rarely exceed 25 μ in diameter.

The wall of the intermediate duct is formed of cubical or flat-cubical epithelial cells which have relatively large rounded or elongated nuclei. Their cytoplasm has no affinity whatever for acid dyes, but rather is slightly basophilic; consequently in haematoxylin-eosin preparations the intermediate duct does not receive a red colour. A few much flattened basal cells appear to represent the basket cells of the terminal secreting part. The narrow intermediate ducts appear as though interposed between the broader secreting parts on the one hand and the stouter secretory ducts on the other. They occur in particularly large numbers in the parotid gland and are much less numerous in the submaxillary
gland. Pl. 45, Figs. 2, 4

These intermediate ducts have one peculiarity, viz. that the cells of their simple cubical epithelium, which generally shows no secretory function, may become so filled with mucus that the intermediate ducts form long, tubular, mucous, glandular structures, in appearance like terminal secreting parts. This is regularly the case in the sublingual gland major and occurs to some extent in the submaxillary gland, where it gives rise to mixed secreting parts.

Pl. 4, Fig. 4
Pl. 45, Figs. 1—3
The **secretory** or **salivary ducts** (also known as striated ducts by reason of the basal striation of their epithelial cells) are distinguished from the intermediate ducts which open directly into them, by the marked increase in their diameter. Both the diameter and the thickness of the wall of the secretory duct steadily increase throughout their course; although the first part of the secretory duct which receives the intermediate duct measures at least 40—45 μ. But they differ from the intermediate duct even more in their structure than they do through the change in diameter. The wall consists of epithelial cells which at first are essentially cubical but which gradually become columnar. These cells are distinguished from those of the intermediate duct not only by their height, but even more by their unusually strong affinity for acid dyes. Consequently in haematoxylin-eosin preparations the sections of the secretory ducts are stained an intense red and stand out clearly in contrast to the terminal secreting parts and intermediate ducts. The pronounced radial striation of the bases of the cells is another characteristic which has already (p. 42) been mentioned. This epithelium shows distinct terminal bars and rests directly upon the membrana propria, except that occasionally isolated, flat, basal cells, a continuation of the corresponding cells of the intermediate duct, may be found between the columnar epithelium and the basal membrane. This highly characteristic part of the
Pl. 4, Fig. 4 arborization of the duct system is especially extensive in the submaxillary gland, somewhat less so in the parotid gland and in the remaining glands is either very greatly reduced or is completely lacking.

The structure of the duct system of the salivary glands changes a second time when the secretory duct with its basal striation terminates in one of the **primary branches** of the main duct. There is no change in diameter at this point for the epithelium of the salivary duct has gradually increased in height; but the epithelium itself changes rather suddenly into a stratified columnar epithelium of two rows of cells. That is to say the basal layer of cells, which in the salivary ducts was almost completely suppressed, now becomes continuous. At the same time the columnar cells lose their basal striation and their affinity for acid dyes becomes noticeably less. Near the opening of the duct this columnar epithelium of two layers passes quite suddenly into a stratified squamous epithelium.

Special Features of the Salivary Glands

a. The Serous Glands of the Oral Cavity

The **parotid gland, glandula parotis,** is — at least in man — a purely serous gland of almost truly alveolar type[1], a compound alveolar gland. The terminal secreting parts
Pl. 45, Figs. 1, 2 have the form of pear-shaped vesicles, which in rare cases are exactly spherical; but which
Pl. 3, Fig. 8 much more often are somewhat elongated and may even be branched. The lumen is extremely narrow, often recognizable only with difficulty. The cells when filled with secretion are high and not particularly dark. The nucleus is small and markedly spherical and rarely lies quite in the centre of the cell, but is usually somewhat near the base. When emptied of secretion the cells are lower (cubical) and darker (opaque). Between the cells there are found rather short secretion canaliculi which end blindly. Each alveolus of the

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[1] The difference between alveolar and tubulo-alveolar is often very slight. Even in the parotid gland there are secreting parts which almost may be termed "short tubular".

parotid gland is covered by a thin membrana propria; basket cells are comparatively rare. The interstitial connective tissue is in itself very poorly developed, yet adipose tissue is almost constantly present, even in situations where the alveoli are closely packed together. Connection with the duct system is established by long, narrow INTERMEDIATE DUCTS. These pass singly into typical SECRETORY (salivary) DUCTS; or several intermediate ducts may unite to form one of somewhat larger diameter, which in turn empties into a salivary duct. The latter ducts may unite to form ducts of larger caliber in which a basal striation in the columnar epithelium can no longer be recognized and whose epithelium soon consists of two distinct layers of cells.

The LINGUAL GLANDS OF EBNER (serous glands of the tongue) resemble the parotid gland although their alveoli are more tubular in shape. They are formed of small, dark, Pl. 44, Fig. 4 cubical cells which even when filled with secretion do not attain either the size or the clearness of the cells of the parotid gland. The zone of the cell next to the lumen is darker than the outer zone which contains the nucleus. Secretion granules are clearly demonstrable only in the inner zone (see Fig. 10, Pl. 3). The cells consequently resemble more the serous cells of the submaxillary gland. The alveoli pass immediately, *i. e.* without the aid of intermediate ducts, into excretory ducts which terminate in the furrows of the circumvallate or foliate papillae. These excretory ducts are lined by a columnar epithelium (or by a ciliated epithelium) of one or two rows of cells; secretory ducts are consequently lacking.

b. The Purely Mucous Glands of the Oral Cavity

These are confined to the areas previously named (p. 195); that is to say they are situated among the lingual follicles. Their ducts are lined by columnar epithelium and usually open into the cavity of the follicle. The secreting cells show the characteristics of mucous cells (p. 194); secretory ducts are absent; basket cells may be seen distinctly. The lumina, as in all secreting parts which produce mucus, are always wide.

c. The Mixed Glands of the Oral Cavity

The human SUBMAXILLARY GLAND, *glandula (salivaris) submaxillaris (submandibularis)*, consists chiefly of two kinds of secreting parts, of which one is purely mucous Pl. 45, Figs. and of alveolar rather than of tubular form, resembling greatly those of the parotid gland (p. 195). These alveoli outnumber the tubulo-alveolar mucous secreting parts which occasionally are almost purely tubular. The latter may be at once distinguished from the purely serous alveoli by their greater diameter and clearer cells, but cannot be said to be purely mucous, although they are predominantly so. For frequently crescent-shaped groups of dark, serous cells are applied either to the blind ends of the tubules (which are commonly forked), or laterally to the mucous cells (crescents of GIANUZZI). Now and then a crescent will be formed of but a single cell, although usually it contains from two to five cells. In addition there occur secreting parts which at first are mucous and then for a short distance become serous.[1] Secretion canaliculi are to be found only between the serous cells, *i. e.* in the purely serous alveoli and in the crescents. Every secreting part in the submaxillary gland is surrounded by a membrana propria and passes into a distinct intermediate duct formed of flat cells. These ducts in turn end in typical secretory (salivary) ducts. The latter resemble those of the parotid gland in having basal striations in their epithelial cells. In no other salivary glands are these ducts so extensive as in the submaxillary glands. Basket cells are common in the mucous secreting parts. The stouter branches of the duct system have an epithelium of two rows of cells; the main duct, ductus submaxillaris, has quite a thick epithelium towards its termination. The interstitial tissue is rich in elastic fibers; while the collagenous tissue is not very abundant and adipose tissue is altogether absent.

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[1] There are marked individual differences in the structure of this gland. Usually the serous character predominates greatly, so much so that mucous (muco-serous) secreting parts are rarely to be found; but occasionally, the latter are present in much larger numbers, which however never approach the numbers of the serous alveoli.

Pl. 45, Figs. 5, 6 The part of the SUBLINGUAL GLAND which discharges its secretion through a single duct, *glandula (salivaris) sublingualis major,*[1] consists of tubulo-alveolar secreting parts which are often forked and twisted, and in places may even be thickened and elongated, thus becoming tubular rather than alveolar. In contrast to the submaxillary gland these secreting parts, almost without exception, show the same structure, that of mucous cells grouped around a relatively wide lumen. They are very sharply distinguished from the mucous tubuli of the submaxillary gland by the greater mass of the serous cells which form the crescents and which in this gland surround a true narrow lumen. Consequently the greater part of the secretion formed by the gland is of mucous character and thus differs essentially from the secretion of the submaxillary gland; nevertheless the gland contains a considerable quantity of serous cells. The latter usually appear in the form of "large crescents", *i. e.* of longer or shorter, blind-ending appendages of the mucous tubules. Isolated purely mucous alveoli occur much less frequently (p. 195). Secretion canaliculi are found only within the crescents and their lumina are very narrow indeed.[2] The duct system is less complex than that of the parotid or submaxillary glands. Intermediate ducts (p. 195) are not present nor as a rule are salivary ducts to be found; although parts of the ducts show a basal striation to a variable extent, but often it is altogether lacking. Nor, in this gland, do these parts often approximate the length attained in the other large salivary glands. The secreting parts consequently pass directly into the finest branches of the duct system. The ducts of smaller caliber have a simple cubical epithelium; while the larger branches display a simple columnar epithelium, which in the main duct *(ductus sublingualis major)* and its immediate branches becomes a columnar epithelium of two layers of cells. The interstitial connective tissue of the gland is rich in lymph cells and often almost gives the impression of diffuse lymphatic tissue. Very few crescents are to be found in the *glandula sublingualis minor* the secreting parts of which are almost purely mucous (p. 195).

Pl. 41, Fig. 3 The SMALLER ORAL GLANDS which are of mixed nature and which may be described
Pl. 42, Fig. 1 as mucous glands with large crescents *(glandulae labiales, molares, buccales, linguales anteriores* — see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II) agree in structure with the glandula sublingualis major.

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[1] The chief part (monostomatic part) of the sublingual gland, *i. e.* the part which discharges its secretion by means of the ductus sublingualis major into the ductus submaxillaris, can usually, but not invariably, be distinguished macroscopically from the "glandula sublingualis minor". It also differs in structure from the latter, which really consists of from five to twenty small glands discharging their secretion through the ductus sublinguales minores (polystomatic part).

[2] Since the crescents are large and the secreting parts are bent, every section of this gland contains cross-sections of crescents which are indistinguishable from sections of serous alveoli. In this case the name crescent is naturally unsuitable; in reality this is a serous gland, whose intermediate ducts secrete mucous (p. 195).

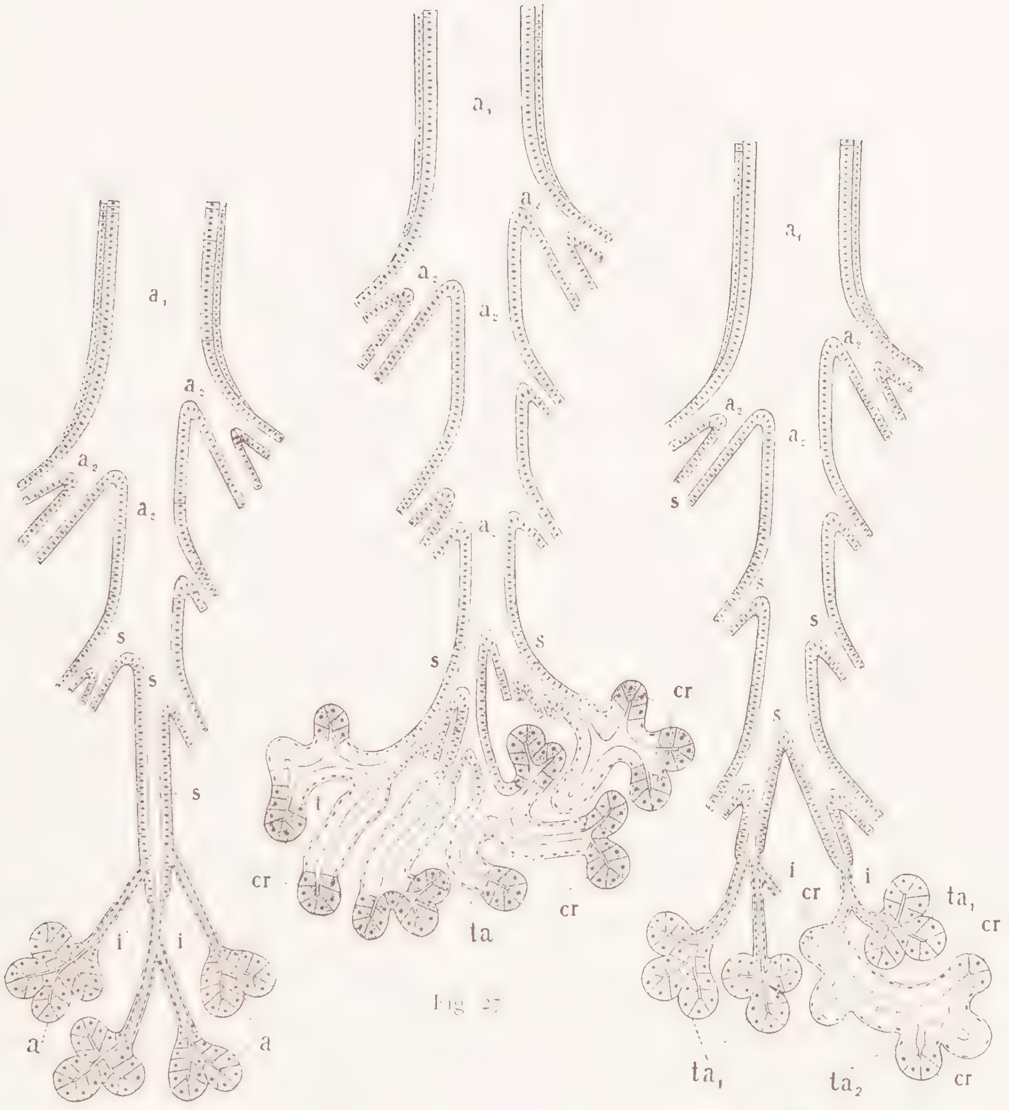

Fig. 26 Fig. 27 Fig. 28

Fig. 26. **Diagram of the Parotid Gland.**
Fig. 27. **Diagram of Sublingual Gland (major).**
Fig. 28. **Diagram of the Submaxillary Gland.**

a = secreting parts of the parotid gland, inclining more to the alveolar than to the tubular type
a_1 = excretory duct of large diameter
a_2 = excretory duct of medium diameter
cr = crescents
i = intermediate ducts
s = secretory ducts
t = secreting parts (branched) of almost purely tubular form
ta = tubulo-alveolar secreting parts
ta_1 = serous secreting parts of rather alveolar form
ta_2 = mucous secreting parts of rather tubular form

The glands of the oral cavity are rich in BLOOD VESSELS whose capillaries are woven about the terminal secreting parts. On the other hand the course of the lymphatic vessels is not perfectly known, true lymphatic vessels having been demonstrated between the larger lobules only. Lymphatic spaces are said to be present between the secreting parts and the capillaries which surround them. These might be considered as the blind beginnings of lymphatic vessels; however the existence of such spaces is not yet sufficiently confirmed. In addition to secretory, non-medullated nerve fibers, there are present in the salivary glands sensory, medullated fibers which have their terminations in the INTERLOBULAR CONNECTIVE TISSUE.

The salivary glands have a double and antagonistic secretory innervation derived from the two salivary nuclei partly through the sympathetic and partly through the parasympathetic (chorda tympani, nervus glossopharyngeus) nervous systems. (For details see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II.) The nerves are numerous and form plexuses which lie between the lobules of the gland and in which a few nerve cells are frequently to be found. From these plexuses delicate fibers run to the secreting parts. According as these fibers terminate on the surface of the membrana propria, or penetrate the latter to reach the glandular cells themselves, they are distinguished as epilemmal or hypolemmal fibers. The majority of the fibers are not only hypolemmal but have their terminations between the cells of the secreting parts.

The fluid secreted by the glands of the oral cavity is commonly known as the **saliva.** It invariably contains organized constituents, tissue elements of the body itself, and parasitic structures. The former are in part desquamated epithelial cells from the oral mucous membrane (p. 201, footnote 3) and in part peculiarly altered, colorless blood cells. The epithelial cells are derived chiefly from the surface of the tongue and are flat, with relatively small, flat nuclei. The parasites described below flourish on these cells, often in large numbers. The colorless blood cells uniformly present in saliva bear the name of SALIVARY CORPUSCLES. They are 10—12 μ in diameter; usually the nucleus has disappeared, while the granular constituents of the swollen protoplasm show the phenomena of BROWNIAN MOVEMENT. The PARASITES growing in the oral cavity and as a consequence occurring quite regularly in the saliva, are in part different forms of bacteria (among them spirillae) and in part mycelia, or threads of a peculiar fungus, Leptothrix buccalis, which grows on the papillae filiformes.

d. The Tongue, *lingua*

Pl. 42, Fig. 4 The substance of the TONGUE consists essentially of the lingual striated musculature[1]
Pl. 43 and of the mucous membrane, *tunica mucosa linguae*, which in almost all parts is firmly
Pl. 44, Fig. 1 and immovably fastened to the muscle beneath by an aponeurotic submucous layer[2] *(fascia linguae)*. The mucous membrane of the tongue is formed consequently of only two layers, 1. the epithelium, a stratified squamous epithelium, and 2. the tunica propria. Beneath the tongue the mucous membrane is an unmodified part of the oral mucous membrane. However in this situation alone, there is a partly developed tunica submucosa which occasionally contains fat cells. On the other hand the mucous membrane covering the dorsum of the tongue shows peculiarities, an anterior "papillary part" being distinguish-

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[1] The muscle fibers are remarkable in having their ends, which are inserted in the fascia linguae, more or less branched (p. 100).

[2] The tongue does not contain a true tunica submucosa in the form of a layer with definite boundaries.

able from a posterior, follicular portion (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II).

The Papillae of the Tongue, papillae linguae

The term papillae as applied to the so-called papillae of the tongue is a misnomer. They are not papillae but villi[1] which themselves bear true papillae, the so-called secondary papillae. In man four main types of the former may be distinguished; *"papillae" filiformes (conicae)*, *fungiformes*, *vallatae* (circumvallatae), and *foliatae*.

Pl. 42, Fig. 4
Pl. 43

The FILIFORM and FUNGIFORM "papillae" are found together over the entire papillary part of the tongue. The circumvallate papillae, on the contrary, are few in number and mark the boundary of the follicular portion, extending in a single row to the posterior lateral margin of the tongue.

The body of a **filiform papilla** consists of a conical basis (papilla conica) of connective tissue rich in elastic fibers; *i. e.* the papilla is broader at its base than at its apex. The conical axis of tunica propria usually is continued into long and pointed "secondary papillae" which often show a circular or horseshoe-shaped arrangement. The number of these secondary papillae is considerable (5—10 and even more).[2] The papillae bear cornified projections corresponding to the secondary papillae[3] and are covered by a thick, stratified squamous epithelium, the upper flattened cells of which are often arranged in many layers. These filiform papillae form the majority of all the papillae of the tongue. Their length varies from one to three mm. Often they form longitudinal rows in which the stout epithelial points of the papillae are directed backward.

Pl. 42, Fig. 4
Pl. 43, Fig. 1

The **fungiform papillae** have broad cores of connective tissue that contains but little elastic tissue. Their upper surfaces bear a number of secondary papillae which usually are not very long; no secondary papillae are to be found on their lateral surfaces. Their epithelial covering is usually quite flat, without cornified points or other projections; moreover it is considerably thinner than the epithelium of the filiform papillae. As a result, during life these papillae appear bright red because their blood vessels, which are remarkably large, show through the comparatively thin epithelium. The papilla is only 1—2 mm. high. Its upper end usually is distinctly broader (0,4—1 mm.) than its base; hence the fungiform appearance. Although taste buds are never present in the fungiform papillae of the middle part of the tongue, in other regions they are found on these papillae during youth, and less frequently in adult life.

Pl. 43, Fig. 1

The **circumvallate papillae**[4] are few in number (usually 7—12) and resemble the

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[1] By papillae are understood projections of connective tissue into epithelium without alternation of the plane of the epithelial surface which remains smooth, *e. g.* papillae of the corium of the skin. Villi, on the other hand, are structures which project beyond the surface, for instance of a mucous membrane, and consist of both connective tissue and epithelium. Normally the skin contains only papillae, not villi; if the latter structures (warts, condylomata) are present they are pathological. True papillae are present in the oral mucous membrane wherever stratified squamous epithelium is found (p. 35).

[2] The number of secondary papillae varies. Usually only three are to be seen in a section, but since only a few of those which project from the whole surface of the connective tissue axis can be involved in one section, the total number is often five or more.

[3] The squamous epithelium of these papillae is arranged in many layers, but is not cornified as in many animals; although the cells contain keratohyalin. They show strong inclination to scale off, consequently epithelial masses partly or entirely desquamated are to be seen in sections. The cells from the ends of these papillae are cast off into the saliva along with bacteria and mycelial threads which hold the cells together in masses.

[4] As to the number and arrangement of these papillae see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II.

Pl. 43, Fig. 2 papillae fungiformes. However they are much broader than the latter, although often lower, and are scarcely narrowed at the base. They are surrounded by a smooth non-papillated wall and by a circular furrow; consequently they are set deeply in the mucous membrane, only their upper surface projecting above the general level of the tongue. Like the fungiform papillae they have secondary papillae, chiefly on the upper surface, but occasionally on the sides. These secondary papillae are usually low. Taste buds (p. 294) lie in the epithelium of the sides of the papillae, and in somewhat smaller number in the opposite wall of the furrow. The connective-tissue core of the circumvallate papillae contains many nerve fibers and scattered nerve cells, or groups of nerve cells and occasionally even smooth muscle. These papillae are only 0.5—1.5 mm. high, but are 1—3 mm.
Pl. 43, Fig. 3 broad.

The degree of development of the human **papilla foliata** is highly variable; although in many animals it is a constant and well developed structure. It consists of parallel lamellar elevations varying in size and number, which alternate with corresponding depressions and contain, like the circumvallate papillae, numerous taste buds in their lateral epithelium. Now and then only one surface of a lamella is set with taste buds, or the latter are distributed among the lamellae at only one particular level; but often fifteen or more buds occur in a row. The papilla foliata and the circumvallate papillae lie in the glandular portion of the lingual mucous membrane, small serous glands emptying into the furrow of the circumvallate papillae, or between the lamellae of the papilla foliata.

The LYMPHATIC STRUCTURES OF THE TONGUE are in part SOLITARY NODULES, *e. g.* in the wall of the circumvallate papillae; but the nodules more commonly occur in groups forming the so-called LINGUAL FOLLICLES, *folliculi linguales.*

The **lingual follicles** are flat, wartlike protuberances of the posterior, non-papillated
Pl. 44, Fig. 1 part of the lingual mucous membrane (base of the tongue). Their diameter measures from one to four millimeters. In the middle lies a narrow, but rather deep, depression, the FOLLICULAR CAVITY. The wall of this cavity consists of lymphatic (adenoid) tissue, with a few secondary lymph nodules and their germ centres, all being sharply marked off from the surrounding muscle and connective tissue.[1] The follicular cavity is lined by the stratified squamous epithelium of the surface of the tongue; but in this situation the epithelium is much broken up by extensive migration of leucocytes (p. 204). Around the lingual follicles and between and beneath them, lie many purely mucous glands (p. 105), which in considerable numbers extend deep into the tongue between the muscle bundles.

The MUSCULATURE of the tongue is composed exclusively of the striated variety of fiber. In general the fibers are of small diameter, but are rich in sarcoplasm and exhibit a peculiar branching just previous to their insertion.[2] Towards the tendon-ends of the muscle fibers nuclei may be observed in both central and superficial (hypolemmal) positions. Then follows the transition to the tendon-like connective-tissue bundles of the lingual fascia.

Pl. 43, Figs. 2, 3 As regards the **lingual glands** those of the dorsum of the tongue must be distinguished from those of its under surface. The former are not present in the mucous coat of the anterior and middle portions of the tongue. They appear first in the gustatory region (see above) where they have a purely serous character and are small and relatively few. Nearer the base of the tongue they are larger, are placed closer together, and are of purely mucous character. On the other hand the only complex of glands in the anterior part of the tongue is of mixed nature. This is the so-called gland of Nuhn (glandula lingualis anterior), actually a complex of small glands which empty upon the mucous membrane of the under surface of the tongue.

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[1] At the base of the tongue adipose tissue is also to be found in the mucous membrane.

[2] See p. 100 and Fig. 8, Pl. 12. In many animals, *e. g.* the frog, the branching of the muscle fibers of the tongue is much more extensive than in man.

The **foramen caecum** linguae usually leads into the rudimentary ductus lingualis which may terminate in mucous glands; but occasionally accessory thyreoid glands (p. 229) are associated with it as well.

The BLOOD VESSELS of the tongue are very abundant. Capillary loops from a plexus in the mucous membrane enter the secondary papillae; capillaries also enter into the lingual follicles. The wide radicals of the veins which pass into superficial venous plexuses are to be found in the larger papillae, that is in the fungiform and more particularly in the vallate papillae. Lymphatic vessels are equally numerous. Their blind ends lie in the papillae (several in the broader papillae), and in the posterior, follicular part of the tongue they surround the lingual follicles with close capillary networks.

The NERVES of the tongue terminate partly (branches of the hypoglossal nerve) in motor end plates upon the muscle fibers. Others (branches of the glossopharyngeal nerve) enter the taste buds of the vallate and foliate papillae. Still others, sensory nerves (lingual nerve), end in simple terminations, or in terminal corpuscles, in the mucous membrane and in the epithelium itself. Groups of sympathetic nerve cells (hemiganglia) are constantly found in the vallate papillae.

2. Palate, Palatine Tonsil, Pharynx

The **hard palate,** *palatum durum*, is formed of a very highly glandular mucous membrane which is firmly attached to the periosteum of the bone by the deeper layer of its tunica propria. The mucous membrane is thicker posteriorly than it is anteriorly and laterally than in the median line. Although a true tunica submucosa is wanting, the mucous membrane of the hard palate has a marked layer of submucous adipose tissue, one to two millimeters thick, particularly noticeable in the regions where the mucous membrane is thicker. The anterior part of this mucous membrane is entirely devoid of glands; posteriorly glands which are purely mucous gradually appear and rapidly increase in number.

The **soft palate,** *velum palatinum*, shows upon its anterior surface turned towards the oral cavity, the character of the oral mucous membrane, *i. e.* a thick, stratified, pavement epithelium with very long papillae. The mucous membrane, which cannot be sharply separated from a submucous coat, contains a very thick, compact layer of mucous glands (p. 195) which often sink deep into the musculature. Between the glands and between their excretory ducts the mucous membrane contains elastic fibers and frequently adipose tissue. However, the latter is not so important a constituent as it is in the hard palate. The posterior surface of the soft palate is turned toward the naso-pharynx and bears over the uvula a thin, stratified pavement epithelium with quite low papillae. Toward the base of the soft palate, *i. e.* towards the nasal cavity, this epithelium gradually passes into the stratified, ciliated epithelium of the latter. The mucous membrane of this surface of the soft palate is also rich in glands, which however are not purely mucous but are mixed glands with crescents. They are confined to the mucous membrane and to the poorly developed submucous layer, and never enter the muscular layer. Small solitary

Pl. 42, Figs. 2, 3

follicles are also to be found as well as diffuse lymphatic tissue. In the middle, between the mucous coats of the two surfaces, there lies the striated musculature of the soft palate, the *m. uvulae* and radiating bundles of the *m. levator veli palatini*.

Pl. 44. Figs. 2, 3

The **palatine tonsil,** *tonsilla palatina*, resembles the lingual follicles in structure but is composed of much greater numbers of lymph nodules. Its lymphatic tissue is sharply marked off from the nearby musculature and mucous glands of the pillars of the fauces. Mucous glands as a rule are practically lacking in the tonsil proper, being pressed aside. Irregular depressions in the surface of the mucous membrane, the *fossulae tonsillares*, extend into the tonsil. Commonly they are enlarged toward their base and as it were branched, or rather provided with sacculations. These depressions are surrounded by lymphatic (adenoid) tissue with many secondary nodules and germ centres and are lined by stratified squamous epithelium. Quite delicate connective-tissue SEPTA extend from the layer beneath the tonsil into the lymphatic tissue in such fashion that the wall of each fossula consists on every side of but a single layer of lymphatic nodules. Thus the tonsil is as it were subdivided into isolated lymphatic lamellae by these connective-tissue septa.

The tonsil does not possess an independent connective-tissue capsule. It is rather to be thought of as embedded in the connective tissue of the tunica propria which forms both the capsule-like sheath and the septa.

Pl. 44. Fig. 3

In the tonsil, as in all structures in which adenoid tissue is combined with epithelium, there is to be observed an invasion of the epithelium by wandering cells. This process is seen most distinctly in areas such as the tonsil and the lingual follicles, which possess a thick stratified epithelium and into which large numbers of leucocytes have entered. There are found, *e. g.* in the tonsillar crypts, places in which the stratified pavement epithelium contains no wandering cells, these adjoin other areas in which the wandering cells lie scattered among the epithelial cells. Next come areas in which wandering cells are to be found in groups within the epithelium; and finally — especially towards the base of the crypt — the cells migrate in such numbers that the epithelium is completely permeated and broken up by them. In the latter case isolated groups of epithelial cells are to be seen among great masses of wandering cells. Early in this process the papillae of the mucous membrane disappear. Later the epithelium increases in thickness because of the numbers of wandering cells present within it. In areas where the number of wandering cells is greater than that of the epithelial cells, the sharp boundary line between epithelium and the lymphatic tissue of the mucous coat becomes blurred. The wandering cells are chiefly lymphocytes formed in the germinal centers of the lymph nodules (p. 88); polymorphonuclear leucocytes are also constantly present.[1] It is to be noted that the tonsils contain only afferent, not efferent, lymphatic vessels.

The wall of the **pharynx** resembles in its structure that of the oral cavity; although it contains a layer of elastic fibers (elastic limiting layer), which separates sharply the mucous membrane from the muscular coat and sends processes between the muscle bundles. The mucous membrane of the middle and lower parts of the pharynx possesses a stratified pavement epithelium, which usually in the upper part — but with individual variations — becomes a stratified ciliated epithelium like that of the nasal cavity. The mucous membrane is rich in lymphatic tissue[1] and in tubulo-alveolar mucous glands which usually are of the mixed variety (p. 198). The lymphatic tissue grows more abundant in the upper part of the organ, forming solitary nodules and, in childhood, a distinct **pharyngeal tonsil**, *tonsilla pharyngea*, which in the main agrees in structure with those of the palate. However it usually blends gradually with the surrounding diffuse adenoid tissue. A true tunica submucosa is lacking in the pharynx, at least in such places as have a muscular coat. In the upper part of the pharynx where the muscular coat is wanting there appears the so-called aponeurosis pharyngis in the place of the submucosa; but the term aponeurosis is not really deserved. Blood vessels, lymphatic vessels and nerves show the same microscopical relations as they do in the oral cavity.

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[1] It is questioned in many quarters whether all the lymphoid cells found in the epithelium of the tonsillar crypts reach the lumen of the crypts, or whether perhaps the lymph cells may not remain permanently or temporarily in the epithelium.

3. The Œsophagus, *oesophagus*

The wall of the œsophagus consists essentially of a mucous coat and a muscular coat to which there may be added a rather poorly defined tunica adventitia. The mucous and Pl. 46 muscular coats are separated by a well developed tunica submucosa. When the œsophagus is empty the MUCOUS COAT, *tunica mucosa oesophagi*, falls into longitudinal folds. Its epithelium is throughout a stratified pavement epithelium with quite long, pointed papillae. It is thus the same type of epithelium as that which lines the oral cavity and greater part of the pharynx; the epithelial coverings of the two organs pass into one another without any intervening boundary. The tunica propria of the mucous coat has a large content of elastic fibers; otherwise it shows no peculiarities apart from small lymph nodules which occasionally are situated around the ducts of the glands. Strictly speaking these are merely more or less sharply bounded collections of lymphocytes and contain no germinal centers. The tunica muscularis mucosae is very well developed. It consists of longitudinal bundles, and being an integral part of the mucous coat follows the latter in its foldings. In the œsophagus it reaches its relatively greatest development; in no other portion of the digestive tract does the muscularis mucosae attain so great a thickness. In the upper part of the œsophagus the individual longitudinal bundles of the layer are loosely arranged and are separated by connective tissue; but in the lower parts they form a compact muscular layer.

The *tunica submucosa* of the œsophagus consists of very loose connective tissue which frequently contains fat, and whose bundles for the most part run in a longitudinal direction. It contains the nerves and larger vessels for the mucous coat and also small MUCOUS GLANDS — simple, branched, tubulo-alveolar glands of purely mucous character. Their excretory ducts penetrate the muscularis mucosae and tunica propria and in the latter are commonly surrounded by lymph nodules. The ducts pass through the pavement epithelium, running obliquely between two papillae to reach the lumen of the œsophagus. The number of the glands is variable but they are never abundant.

In addition to the mucous glands, other œsophageal glands are quite constantly present which resemble the pyloric glands of the stomach to an extraordinary degree. However they appear more highly branched than the pyloric glands and occasionally even contain scattered parietal cells (p. 207), resembling in this regard the glands of the fundus of the stomach. These glands are found particularly near the entrance into the stomach and in the adjacent part of the stomach itself (see below), and on this account are known as CARDIAC GLANDS. But at times they are found in other areas of the œsophagus, very commonly (in almost 70% of cases) even in the upper portion. In contrast to the mucous glands they always lie in the tunica propria and are often assembled in groups. Their excretory ducts pass through the apices of papillae.

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[1] As in the œsophagus, accumulations of lymphocytes are common around the excretory ducts of the glands. The amount of adenoid tissue is especially great in the region of the ostium pharyngeum tubae auditivae, giving rise to the term tubal tonsil.

The MUSCULATURE of the œsophagus is of mixed character. In the upper portion (about $^{1}/_{3}$) it is composed of striated elements only; in the middle of both striated and smooth fibers, and in the lower third of smooth fibers alone. There is a distinct inner layer of circular muscle and an outer longitudinal layer which at first is strong but which grows steadily weaker towards the lower end of the œsophagus.[1]

The muscular coat is surrounded externally by connective tissue which is continued into the interior of the coat, separating the individual muscle bundles. It represents a poorly defined tunica adventitia.

Blood and lymphatic vessels are abundant in the œsophagus. The veins and lymphatic vessels typically form plexuses[2] in the tunica submucosa and in the tunica muscularis. Slender capillary loops pass into the papillae of the tunica propria.

The nerves which consist in part of medullated and in part of non-medullated fibers show a similar arrangement to those of the stomach and intestine (see below). They first form between the two subdivisions of the muscular coat a plexus which contains numerous sympathetic nerve cells, and from which is derived the innervation of the musculature; while other fibers pass into the submucous tissue and here form another plexus in which are scattered nerve cells. From this plexus there is derived the motor innervation of the tunica muscularis mucosae, so strongly developed in the œsophagus. It also supplies fine sensory fibers to the mucous coat.

4. The Stomach, *ventriculus*

Pl. 47
Pl. 48, Figs. 1, 2 The WALL OF THE STOMACH shows, in general, the same layers as does that of the œsophagus. However the stomach is covered by the peritoneum, consequently a tunica serosa and a subserosa, must be added to the number of the coats.

Pl. 47, Fig. 7 The EPITHELIUM of the surface of the stomach also lines the entire extent of the gastric crypts (*foveolae gastricae*, see below) and is a rather high columnar epithelium. Its cells have a length of 20—30 μ and are relatively narrow. Their ends which are towards the free surface are filled with mucus causing them to resemble goblet cells. However there is an essential difference in the manner of the formation of the mucus in the two types of cells; those of the stomach never assume the characteristic gobletlike form and do not die after secreting the mucus (p. 209). According to the stage of secretion the basal part of the cell, which contains the nucleus but which does not produce mucus, may be either high or low and the nucleus either round or flat. The mucus first appears as a distinctly granular antecedent which quite fills the part of the cell next to the lumen. The transition from the thick, stratified, squamous epithelium of the œsophagus to the relatively much lower simple columnar epithelium of the stomach is quite abrupt, the inner level of the surface falling sharply along a boundary line which usually is uneven and jagged. At this point the stratified squamous epithelium which began in the oral cavity and continued throughout the pharynx and œsophagus comes to an end.

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[1] A few bundles of longitudinal muscle are occasionally found on the inner side of the muscular coat. Toward the lower part of the œsophagus the layer of circular muscle becomes steadily thicker at the expense of the longitudinal layer. The boundary between striated and smooth muscle varies in different individuals, thus even in the lower part of the œsophagus there occasionally are present isolated fibers of striated muscle.

[2] The cushion-like swelling on the posterior wall of the upper part of the œsophagus is produced by a venous plexus.

The tunica propria of the stomach beneath the bases of the gastric crypts contains TUBULAR glands, several of which empty into each foveola; very little interstitial tissue is found between the glands. This interstitial tissue consists rather of reticular than of fibrillar connective tissue and is rich in lymph cells (also in plasma and other cells) particularly in the region of the pylorus where the glands are less closely packed together. In the latter situation there are also commonly found solitary nodules (so-called "glandulae" lenticulares), which however are present to some extent in the rest of the gastric mucous membrane, although rather rare in the region of the fundus. The nodules have typical germinal centers but usually show an irregular form and, in contrast to the intestine (see below), are situated exclusively in the tunica propria. (As to the smooth muscle fibers in the tunica propria see below.) Heavier layers of interstitial tissue are to be found in the fundus region but superficial to the zone of the glands and at the level of the gastric crypts, whose walls so to speak, they form.

The gastric glands differ in the chief regions of the stomach (cardiac portion, fundus and body) from those which lie in the pyloric region. The boundary of the two regions as regards the distribution of the glands is by no means sharp. Accordingly FUNDUS GLANDS, *glandulae gastricae propriae* and PYLORIC GLANDS, *glandulae pyloricae*, are to be distinguished. Since the glands form the greater part of the mucous coat they impress the latter with their typical characteristics; consequently the terms pyloric mucous membrane and mucous membrane of the fundus are used.

In the REGION OF THE FUNDUS the broad gastric crypts are lined by the superficial Pl. 47. Figs. 2—6
epithelium, but are not so deep in proportion to the thickness of the mucous coat as are those of the pyloric region. They measure from 150—250 μ in depth according to the condition of contraction or relaxation of the musculature. The glands of the fundus region are tubules ½—1½ mm. long, slightly branched and bent only at their bases; neighboring glands may anastomose. The narrowed necks of the glands open into the bases of the crypts, while at their blind ends the glands are slightly expanded. They penetrate the entire thickness of the tunica propria down to the muscularis mucosae. The fundus glands contain two types of cells known as CHIEF CELLS and PARIETAL CELLS. The former are small cells, approximately cubical or low-columnar. In fixed and stained preparations their protoplasm appears scarcely colored, only the relatively large nucleus being very evident; but in the living condition they contain the coarsely granular antecedents of pepsin. The PARIETAL CELLS are large, irregularly flattened, spherical or polyhedral cells whose protoplasm stains intensely with acid aniline dyes and is distinctly of a finely granular appearance. They frequently contain two nuclei. The parietal cells are found in abundance between the chief cells in the so-called necks of the glands (*i. e.* the parts of the glands emptying into the foveolae) where their number is equal to or greater than that of the chief cells. In the body of the glands they are scattered and are very few in the somewhat expanded and slightly bent fundus of the gland (*i. e.* in the blind end of the glandular tubule). The last named portion of the gland consequently is formed entirely of chief cells. Intracellular secretion canaliculi are present in the parietal cells. If the parietal cell has

Pl. 4, Fig. 11 been pressed away from the main lumen the latter establishes connection with the secretory canaliculi by a short lateral extension; this as a rule occurs in the deeper portions of the gland.[1] The intracellular secretion canaliculi of these large cells form basketlike networks in the cytosome (see Fig. 11, Pl. 4). No secretion canaliculi are to be found in connection with the chief cells.

The PYLORIC GLANDS end in narrow, deep crypts 300—350 μ in length. The glands Pl. 48, Figs. 1, 2 are essentially shorter than those of the fundus; they branch more and are more strongly bent at the base. They are not purely tubular but are rather tubulo-alveolar. They contain but one type of cell which bears only a superficial resemblance to the chief cells of the fundus glands and really differs from them in several respects. In form they are cubical to columnar; the nucleus is flattened against the basal surface of the cell; the protoplasm is rather clear. Intercellular secretion canaliculi are present and the glands greatly resemble the cardiac glands. Apparently no mucous secretion takes place in spite of an outward resemblance of these pyloric cells to the mucous cells of the oral mucous glands. The epithelium of the gastric glands is surrounded externally by a membrana propria which contains flat, elongated cells.

The parietal cells apparently secrete the hydrochloric acid of the gastric juice, the chief cells, and perhaps also those of the pyloric glands (?), the pepsin. Consequently the old name, rennet glands, for the glands of the fundus type should be discarded. Granules appear within the cells of the pyloric glands as antecedents of their secretion.

The CARDIAC GLANDS already mentioned should be associated with the two chief types of glands and their zones in the stomach. In structure they resemble rather the glands of the pylorus and are to be found partly in the lowermost region of the oesophagus and partly in the region of the stomach immediately adjacent.

Pl. 47, Figs. 1, 2 Pl. 48, Fig. 1 The tunica MUSCULARIS MUCOSAE of the stomach usually shows two distinct layers, an inner circular layer and an outer layer of longitudinal fibers. Occasionally even three layers are to be found, the outermost being again a circular layer. In the pyloric region the muscularis mucosae is stronger than in the fundus, but even here does not attain the strength which it does in the oesophagus; although in the latter it is of only one layer. Isolated groups of fibers separate from the main layer and turn upward into the mucous membrane between the glands as far as the bases of the crypts. These fibers are most abundant in the region of the pylorus. The tunica SUBMUCOSA resembles that of the œsophagus, being formed of loose connective tissue with elastic fibers and occasional small masses of adipose tissue. It also contains the blood vessels and nerve trunks for the mucous coat.

The stout tunica MUSCULARIS of the stomach consists entirely of smooth muscle which in the main is arranged in two layers, an inner circular and an outer longitudinal. These layers are especially thick and well defined at the pylorus. To these is added a radiation of the musculature of the œsophagus, which causes the layers of muscle in the cardia and body of the stomach to become decidedly complicated (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II).

The tunica SEROSA of the stomach bears on its surface the flat serous epithelium but otherwise shows no peculiarities.

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[1] Hence the name parietal cells, *i. e.* wall cells, cells not of the same layer as the chief cells but apparently external to them.

5. The Small Intestine, *intestinum tenue*

The SMALL INTESTINE shows in general the same layers as are present in the stomach Pl. 48. Figs. 3—5
and in its whole course presents a very uniform structure, complicated only in the duodenum Pl. 49
by the presence of the duodenal glands. Pl. 52, Fig. 1

The mucous membrane of the small intestine is distinguished by the presence of villi, *i. e.* of filamentous projections of the mucous coat (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II). The VILLI INTESTINALES begin in the duodenum as long, large, and somewhat flattened structures which may occasionally be present in the stomach close to the pylorus and which extend as far as the ileo-colic valve. The villi of the ileum are decidedly smaller and more cylindrical, being even conical; while those of the jejunum are shaped more like a leaf. They consist of filamentous processes of the mucous coat which are covered by epithelium and which may reach from ½ 1 mm. in length.

The EPITHELIUM of the entire digestive tract from pylorus to anus is a simple columnar epithelium (p. 34) of an average thickness of 30 μ. Its cells bear a distinctly striated cuticular border on their free surface; the elongated nucleus lies in the basal, usually slender, half of the cell. For the cells naturally become narrowed where they cover curved surfaces; and the intestinal surface usually is curved. GOBLET CELLS (p. 43) are present in variable numbers. Both goblet and ordinary cells are to be found in the proximal parts of the short, tubular intestinal glands (glands of Lieberkuhn) which lie in the tunica propria
of the small intestine. In the small intestine these glands measure only 0.15—0.2 mm. in Pl. 49
length. However the columnar epithelium of the glands is decidedly thinner than that of Pl. 52, Fig. 1
the villi, scarcely 20—30 μ. The cuticular border of the glandular epithelium is less distinct and at the bottom of the glands is altogether lacking.

The epithelium rests upon a structureless BASAL MEMBRANE whose connective-tissue origin cannot be mistaken since occasionally it clearly contains nuclei. Leucocytes which have wandered into the epithelium are frequently to be seen. The epithelium shows definite peculiarities only at the bases of the glands of Lieberkuhn. The deepest cells which form the very fundus of the glands contain distinct secretion granules which are easily demon-
strated by the use of different stains, *e. g.* acid aniline dyes; these are the so-called cells Pl. 3. Fig. 10
of Paneth.[1] The figures of mitotic cell division are quite uniformly to be observed in those Pl. 48, Fig. 5
cells of the gland which lie next above the CELLS OF PANETH. It is generally accepted that these divisions serve to regenerate the intestinal epithelium; consequently the latter moves from the depths of the glands towards the surface of the villi. This regeneration is rendered necessary by the death of the goblet cells (see below). The latter extend into the necks of the glands, but in the small intestine they are chiefly situated on the sides of the villi.

The TUNICA PROPRIA of the small intestine fills the narrow spaces between the short
intestinal glands and also forms the basis of the villi. In the longitudinal axis of the latter Pl. 49, Fig. 4
lie the CENTRAL OR AXIAL LACTEAL VESSELS which form the radicals of the lymphatic Pl. 53, Fig. 2
vessels of the small intestine. In addition the villi contain blood capillaries and a small amount of connective tissue which is of reticular rather than of fibrillar nature and is rich in lymph and plasma cells. Although the fibers are by no means abundant, precollagenous fibers are present and may also be demonstrated in the wall of the lacteal. A few elastic fibers are also to be found and some fibers of smooth muscle which extend from the muscularis mucosae into the villi. At the free end of the villus these fibers curve and come

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[1] Other granules are also to be observed in these cells.

Pl. 49, Figs. 2—4 together thus forming a tubular network within its stroma. The part of the tunica propria lying between the intestinal glands is rich in leucocytes and eosinophiles but shows no other peculiarities.

The *tunica muscularis mucosae* of the small intestine is well developed and usually consists of two layers, the inner being circular and the outer longitudinal. A few fibers turn from the muscularis mucosae into the villus for the purpose of emptying the axial lacteal of its contents. The contraction of these muscle fibers often produces in preparations marked changes of the form of the villi, such as folds in the epithelium, retraction of the interior of the villus from its epithelial tube etc.

The very plastic TUNICA SUBMUCOSA of the intestine contains, in addition to unusually loose connective tissue and elastic fibers, both blood vessels and a nervous plexus (p. 212). The *plicae circulares* (Kerkring's folds) are folds of the entire mucous membrane including the muscularis mucosae.[1] Blood vessels are contained in the thin prolongations of the tunica submucosa which extend into the folds. Pl. 49, Fig. 1

The MUSCULAR COAT, *tunica muscularis*, of the small intestine falls into two distinctly separated layers, a strong inner circular and an outer longitudinal layer. The latter is covered by the tunica serosa as in the stomach. Within and between the two muscular layers lie many elastic fibers and a nerve plexus (p. 212).

The structure of the first part of the duodenum differs from the description just given Pl. 48, Figs. 3, 4 inasmuch as the DUODENAL GLANDS present in the tunica submucosa render the picture of the intestinal wall more complicated. These duodenal glands (also named Brunner's glands), *glandulae duodenales*, unlike the intestinal glands are not simply straight tubules but are much branched and twisted simple tubular glands. Their cells resemble greatly those of the pyloric glands and like them have a marked resemblance to the mucous cells of the salivary glands, to which apparently they are closely related, since they occasionally give the reactions of mucus. Their excretory ducts penetrate the tunica muscularis mucosae and tunica propria and open either on the surface of the mucous coat or into an intestinal gland. In man frequently a considerable part of the duodenal gland in the neighborhood of the duct lies internal to the muscularis mucosae, *i. e.* within the mucous coat.

In the upper part of the duodenum the Brunner's glands form an extensive glandular complex which is subdivided by connective-tissue septa and occupies almost the entire thickness of the submucosa. Towards the middle portion of the duodenum the glands become decidedly smaller and only touch the muscularis mucosae without passing on deeper into the submucosa. As is shown by longitudinal sections through the pyloric region there exists a direct continuity between the closely related pyloric glands on the one side and those of the duodenum on the other; as a result it is often impossible to determine the boundary between them.

6. The Large Intestine, *intestinum crassum,* and the Rectum, *rectum*

Pl. 50 The structure of the wall of the LARGE INTESTINE and of the rectum is at once distinguished from that of the small intestine by the absence of villi. Moreover the intestinal glands are longer, even twice as long as in the small intestine (0.4—0.7 mm.). They increase in length from the caecum toward the rectum, the caecal glands being quite short, scarcely longer than those of the small intestine. Numerous goblet cells are usually present and extend almost to the base of the gland, but are most abundant in its middle portion; while on the surface and in the mouths of the glands the epithelium contains few goblet cells. This is in marked contrast to conditions in the small intestine where the epithelium of the villus shows the most goblet cells. The granular cells of Paneth are wanting. On the other hand the base of the gland shows numerous mitoses supplying cells to replace the numerous dying goblet cells. Young goblet cells are mostly found near the base of the glands.

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[1] See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II.

The longitudinal muscle of the large intestine — apart from that of the rectum — is arranged in three strips or bundles, the *taeniae coli*. Between the taeniae the longitudinal muscle is represented by only a few thin bundles.

Except in the points mentioned above neither the mucous nor muscular coats of the large intestine differ in structure from those of the small intestine.

7. The Lymphatic Structures of the Intestine

Pl. 49, Fig. 3
Pl. 50, Figs. 2, 4
Pl. 53, Fig. 1

The mucous coat of the intestine contains in general large numbers of lymph cells which in places are massed together forming special lymphatic or adenoid structures. These are partly SOLITARY FOLLICLES, *noduli lymphatici solitarii*, partly aggregated follicles or PEYER'S PATCHES, *noduli lymphatici aggregati*. The latter structures are found only in the lower portion of the ileum; while the former occur throughout both large and small intestines, but are more abundant in the large intestine and ileum than in the jejunum. The solitary follicles of the small intestine, like those of the stomach, lie altogether within the mucous coat. Villi are absent over their somewhat conical apices which are fused with the epithelium. In the large intestine the broader and larger portions of the pear-shaped follicles lie in the tunica submucosa. Originally these follicles developed within the mucous membrane but later many of them broke through the tunica muscularis mucosae (see *Fig. 2*, *Pl.* 50). Goblet cells are lacking in the epithelium which covers these follicles. The nodules usually, but not invariably, contain germinal centers. In size they vary between 0.2 and 2.5 mm.

Pl. 53, Fig. 1

PEYER'S PATCHES are elongated structures situated in that part of the intestinal wall which is opposite to the mesenterial attachment and consist of ten to sixty associated solitary follicles fused together by their marginal zones.[1] The follicles are somewhat flattened and lie in a single layer which as a rule is almost entirely within the tunica submucosa. Only their apices, like broad lymphoid papillae, project through the mucous coat into the intestinal lumen. True villi are absent over Peyer's patches.

Pl. 50, Fig. 4

The VERMIFORM APPENDIX, *processus vermiformis*, is somewhat similar to the above. In it the mucous coat is rudimentary, containing only a few glands, while the lymphatic tissue greatly predominates and assumes the form of closely adjacent solitary follicles which usually have well developed germinal centers. The solitary follicles and other lymphatic structures of the intestines, at least in man (see below), contain no lymphatic vessels but only blood capillaries.

At the points where the tops of the solitary or aggregated follicles touch the intestinal epithelium the latter is penetrated by wandering cells in a manner which recalls the epithelium of the tonsillar or lingual crypts. In these situations goblet cells are never present. In almost all parts of the intestinal tract there are present within the columnar epithelium occasional wandering cells, probably derived from the diffuse lymphatic tissue of the mucous membrane. This migration of leucocytes is very pronounced in the epithelium of the vermiform appendix whose narrow lumen is often quite filled with them.

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[1] See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II.

8. Blood and Lymphatic Vessels, and Nerves of the Stomach and Intestine

The vessels and nerves show very similar relations in both stomach and intestine. The ARTERIES enter from the mesentery and lie at first in the subserous tissue. They give off branches to the muscle and form in the tunica submucosa a close network, branches of which supply the mucous coat.[1] The glands are surrounded by delicate capillary networks which are most pronounced at the surface of the mucous coat. In each villus of
Pl. 52, Fig. 1 the small intestine there is an arteriole (or several arterioles in the larger villi) which forms a capillary plexus immediately beneath the epithelium. Near the free end of the villus this plexus gives rise to a small vein which takes an axial course. In the stomach and large intestine the VENOUS RADICALS of the mucous membrane have a superficial position and arise from the capillaries which are particularly wide around the mouths of the glands.[2] In the mucous coat the small veins form a superficial plexus, which in the stomach lies beneath the crypts around the necks of the glands.

The LYMPHATIC VESSELS of the small intestine begin in the villi as the axial lacteals, and in the stomach and large intestine as wide lymphatic capillaries between the glands.
Pl. 53, Fig. 2 Capillaries which are particularly broad and flat form networks around the solitary lymph nodules and Peyer's patches. In the mucous coat the lymphatic capillaries form a small-meshed plexus which passes into the large-meshed lymphatic plexuses of the tunica submucosa and muscular coat. The principal plexus is that which lies between the two layers of the muscular coat. The larger vessels run in the subserous tissue to reach the mesentery.

The NERVES of the stomach and intestine are derived chiefly from the sympathetic system and to some extent indirectly from the n. vagus. For the most part they consist of non-medullated fibers which in the gastro-intestinal wall form two plexuses with small
Pl. 36, Fig. 5 ganglia at the points of intersection. The larger plexus, the *plexus myentericus* (of Auer-
Pl. 37, Fig. 1 bach) lying between the circular and longitudinal layers of muscle has large ganglia with multipolar nerve cells and rather regular polygonal or rhombic meshes. It supplies both layers of muscle and the adjacent blood vessels.[3]

The *plexus submucosus* (of Meissner) is much more delicate and less regular. Its meshes are much smaller. It supplies the tunica muscularis mucosae and remaining struct-
Pl. 36, Fig. 4 ures of the mucous membrane and thus contains both motor and secretory, and perhaps
Pl. 48, Fig. 4 also sensory (?), fibers. Both plexuses have ill-defined beginnings in the œsophagus and extend as far as the rectum. They are connected with one another by fine non-medullated nerve fibers which pass through the layer of circular muscle.

9. The Liver, *hepar*

Pl. 51 The LIVER is a large compound tubular gland, the tubuli having a peculiar netlike
Pl. 52, Figs. 2—4 arrangement and being devoid of lumina. The original tubular secreting parts have lost
Pl. 53, Figs. 3—5 their sharp demarcation and appear as reticular and anastomosing groups of cells, forming a so-called reticular gland. In man, and in nearly all of the higher animals, the originally tubular structure of the liver is very difficult to recognize in the fully developed gland, since the character of separate independent tubuli has been almost entirely lost. At the same time intimate relationships with the vascular system have been established which

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[1] The small arteries of the intestinal wall are terminal arteries.

[2] By many these are considered to be venous radicals in spite of the capillary-like structure of their wall.

[3] The cells of these ganglia as a whole are naturally cells of the sympathetic system (p. 119).

completely dominate the arrangement of the secreting parts. Description of the structure of the liver will first be given and later a comparison with the typical tubular gland.

The liver is provided with a connective-tissue capsule, *capsula fibrosa* (of Glisson), which contains elastic fibers and which extends from the porta of the liver into the interior of the organ in company with the vessels, as a cord of connective tissue which divides repeatedly into branches of slowly diminishing diameter. In many animals, *e. g.* the pig, each so-called hepatic lobule — for the substance of the liver may be resolved into lobules — is surrounded by the connective tissue of Glisson's capsule. However, in man the connective tissue of the liver is much less developed and serves only to a small extent to indicate the boundaries of neighboring lobules.

The HEPATIC LOBULES, *lobuli hepatis*,[1] are structures of highly variable form but frequently are prismatic or short-cylindrical. They have a length of 1 ½—2 mm., a breadth Pl. 51, Fig. 1 of 1 mm. and in transverse section appear polygonal. However in addition to lobules of Fig. 29 short columnar form there are others which are club-shaped etc. They consist essentially of trabeculae of cells (so-called liver cords) which anastomose and form a network, the trabeculae being in general arranged radially around the axis of the lobule. This axis is formed by one of the slender radicles of the hepatic veins, the so-called central vein. The lobules of the human liver are not marked off from one another by connective tissue but by smaller branches of the portal vein which form, as it were, vascular sheaths around the lobules. Accompanying the larger branches are small amounts of the connective tissue of Glisson's capsule.

Each liver cord is composed of rows of liver cells; the latter are large (15—30 μ), irregular, polyhedral cells, rich in protoplasm but devoid of membranes. However there is Pl. 51, Fig. 2 a superficial condensation of the protoplasm forming a firm exoplasm which enables the liver cells to act as walls for the bile capillaries (see below). The nuclei are relatively small and not infrequently are two in number. In the fresh condition the liver cells are distinctly opaque and granular due to the presence of granules of glycogen.[2] In addition they usually contain fat in larger or smaller droplets, and frequently pigment (bile pigment) as yellowish or brownish granules. Such cells in enormous numbers (billions) form the parenchyme of the liver.

Neighboring liver cells are in immediate contact and thus form LIVER CORDS (trabeculae) which consist of one or two rows of cells and which anastomose with neighboring cords. The cells retain their places without the aid of a membrana propria; consequently only bare rows, chains and networks of cells are to be seen. As has already been mentioned the arrangement of these cords of liver cells in the lobules is determined by the behavior of the blood vessels.

The **portal vein,** *vena portae*, is an afferent vessel of the liver. The relatively small artery (ramus hepaticus arteriae hepaticae propriae) supplies only the wall of the bile ducts Pl. 52, Fig. 2 and the connective tissue of Glisson's capsule. Its capillaries[3] pass directly into the smallest branches of the portal vein. The latter, *venae interlobulares*, run between the lobules in company with the scanty connective tissue, with the small arteries supplying the walls of the bile ducts and with the small bile ducts themselves *(ductus biliferi interlobulares)*. The capillaries of each lobule are derived from several interlobular veins of varying diameter.

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[1] It will appear from the following description that the hepatic lobule does not at all correspond to the lobule of other glands.

[2] In ordinary, fixed preparations the glycogen has dissolved, leaving in its place vacuoles in the protoplasm of the liver cells.

[3] In circulating through the liver the blood enters by one vein, the portal vein, and is drained away by another vein, the hepatic vein. Consequently the hepatic circulation has at times been characterized as a large venous rete mirabile whose network proper is formed of vessels of capillary structure, such as also form the loops of the arterial rete mirabile in the renal glomeruli. To be consistant any other so-called portal circulation (*e. g.* that of the vitelline vessels of the embryos of teleost fishes) must also be designated as a venous rete mirabile. However in this description the customary term, hepatic capillaries, is considered to be justified and is used.

The interlobular veins send into the lobule from its periphery numerous wide (9—10 μ) Pl. 52, Fig. 2 capillaries which anastomose abundantly and run towards the centre of the lobule in the Figs. 30, 31 meshes of the network of liver cords. In the axis of the lobule lies a small vein known from its position as the central vein, *vena centralis*, of the lobule. These central veins as a whole are the radicles of the efferent venous system, the main trunk of which is the hepatic vein, *vena hepatica*. The central veins receive the capillaries which are derived from the interlobular veins and which have formed a network between the liver cords.

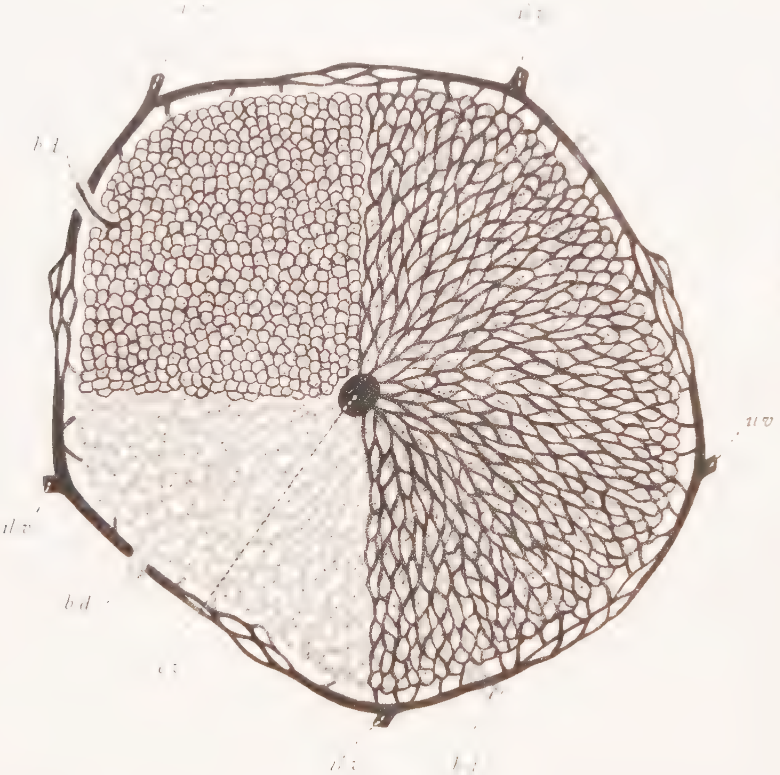

Fig. 29. **Diagram of the Structure of an Hepatic Lobule.**

The lobule is represented in cross section. In the middle is the central vein. Five interlobular veins reach the margin of the lobule which they encircle by their capillary anastomoses. In the right half of the figure the blood capillaries of the lobule are represented in black. In the left upper quadrant the bile capillaries are shown as finer black lines. In the left lower quadrant only the network of the bare liver cords is to be seen (grey). The beginnings of the interlobular bile ducts and their connection with the hepatic cords are also represented in grey.

b d = bile duct
c v = central vein
il v = interlobular vein

The central vein lies exactly in the axis of the lobule at the free end of which (see diagram) it is formed by the confluence of capillaries and appears as a venule. No matter how the length of the lobule may vary, the central vein always lies at about the same distance from the interlobular branches of the portal vein. During its course through the lobule it collects blood from the capillaries on all sides, consequently it has increased considerably in diameter when it arrives at the base[1] of the lobule. Thus each hepatic lobule consists essentially of liver cords and of the blood capillaries which lie between them. The latter are in immediate contact with the cells and usually run along their edges.

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[1] This term is applied to the slightly flattened, broader end of the columnar hepatic lobule. Usually the base rests against one of the larger radicles of the hepatic vein (sublobular vein).

The hepatic lobules actually represent the smallest functional structural units of the liver, but are not so sharply marked off from one another as the foregoing description might seem to imply. They form larger or smaller complexes, so-called lobule groups, within which there lies a central vein of larger order, the SUBLOBULAR VEIN. Each radicle Fig. 30, 31
of this more or less branched sublobular vein, *i. e.* each true central vein, is surrounded by the substance of an hepatic lobule. The central veins may be bifurcated at their blind ends. Several sublobular veins unite to form a larger unit, the collecting vein.

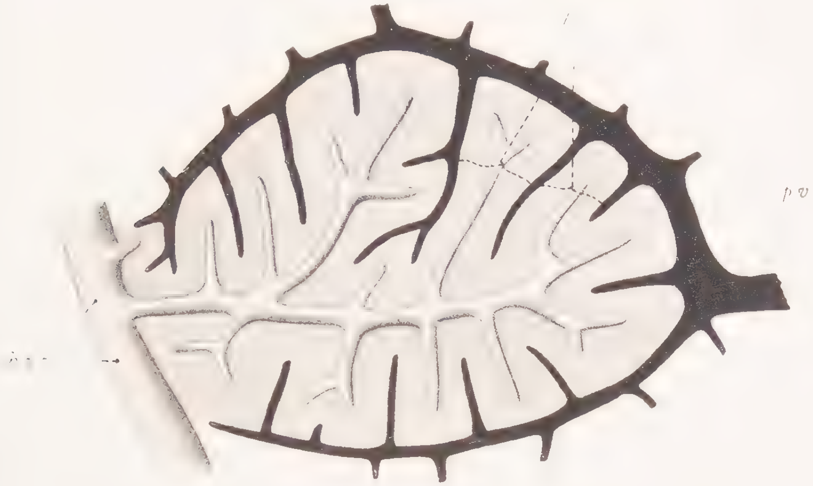

Fig. 30. **Diagram of a So-called "Sublobular VeinUnit"** (after PFUHL)

On the left is a branch of the hepatic vein receiving a large sublobular vein; the latter in turn is formed of smaller sublobular veins into which open the central veins of numerous lobules. (All these radicles of the efferent veins are shown in light grey.) On the right is seen the bifurcation of a large division of the portal vein. From the two subdivisions arise branches, so-called interlobular veins. (The afferent system of veins is shown in black, the substance of the hepatic lobules in dark grey.)

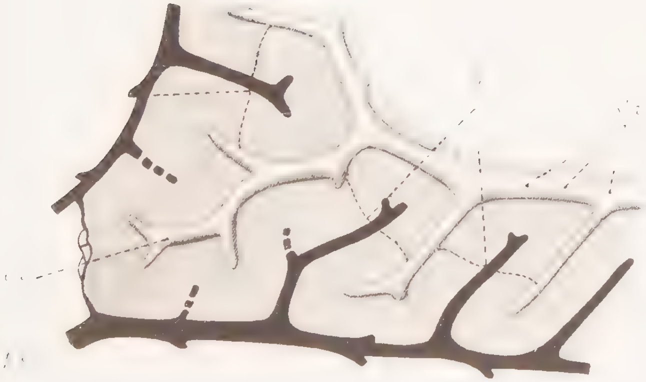

Fig. 31. **Diagram of Lobules and Veins of the Liver** (after PFUHL)

Above is a sublobular vein which receives a number of central veins (light grey). Below and at the left branches of the portal vein give off interlobular veins black). Hepatic lobules are dark grey.

lo = hepatic lobules
c v = central vein
p v = branch of portal vein
h v = branch of hepatic vein, collecting vein
sl v = sublobular vein

In the human liver, as already mentioned, the interlobular branches of the portal vein determine the boundaries of the lobules. They are derived from a large branch of the portal vein and as numerous small pre-capillary veins surround the lobule on all its sides. Pl. 52, Fig. 2
Their terminations do not anastomose directly on the surface of the hepatic lobules but

Pl. 51, Fig. 1 are connected by wide perilobular capillaries. Consequently the liver cords of neighboring lobules are in contact at the periphery of the lobules. Since the branches of the portal vein are accompanied almost to their extreme ends by small arterial branches and by the interlobular bile ducts, and since all these are surrounded by extensions of connective tissue from Glisson's capsule, a certain amount of interlobular connective tissue appears around the larger branches of the portal vein. As a consequence of its extremely small amount in the human liver this interlobular connective tissue appears like an island in a section. On the other hand no trace of interlobular connective tissue is to be seen around the very smallest branches of the interlobular veins nor about the perilobular capillaries. This is in contrast to the liver of the pig in which connective tissue is present in these situations, forming as it does a complete boundary for the lobule.

In addition to the above, there are still other constituents of the hepatic lobule which can be rendered visible only by special means. In the first place there is a delicate intralobular framework of connective tissue which consists of a very fine network of fibers Pl. 53, Fig. 5 woven around the capillaries. Since these fibers become evident only after the employment of special methods of staining, in particular of silver-impregnation methods, they are precollagenous (argyrophile), **reticulum fibers.** Corresponding to the small possibility of displacement within the hepatic lobule these fibers are present in extremely small numbers. However although they support the capillaries it is only around the central vein that they form a layer of noticeable thickness.

A second constituent of the hepatic lobule is represented by the so-called **stellate cells** Pl. 53, Figs. 3, 4 of KUPFFER which are peculiar connective-tissue elements, concerning which there is at present a difference of opinion; but which most probably belong to the reticulo-endothelial system (p. 96). The walls of the hepatic capillaries show a peculiar structure inasmuch as the endothelium has remained in the syncytial stage of embryonic development, and neither cell boundaries nor an absolutely complete capillary wall are demonstrable.

The stellate cells are primarily distinguished from the remaining elements of the endothelial syncytium in having very great phagocytic powers; for instance, they take up foreign bodies, such as granules of ink, from the blood stream in a comparatively short time and can then be recognized very easily. They may be distinguished from those of the rest of the capillary syncytium by their large, clear nuclei. The shape of the stellate cells does not always correspond to their name, but is highly variable. However, they frequently possess processes and in the margin of the lobule they lie by preference at the angles where capillaries divide. In the central part of the lobule their form is often elongated and they are chiefly located opposite the termination of capillaries.

Probably a distinction may be made between grasping situations and digesting situations on the part of the stellate cells. In grasping situations they lie at points which are placed most favorably for removing foreign bodies from the blood stream while in digesting situations they seem to retire to more sheltered places in the capillary wall (?).

The third element of the hepatic lobule, and one which can be recognized only with Pl. 52, Figs. 3, 4 difficulty, is formed by the so-called **bile capillaries,** very slender passages lying between the liver cells, without walls of their own, and terminating in the INTERLOBULAR BILE DUCTS (see below). These are in truth only INTERCELLULAR SECRETION CANALICULI (p. 45). They are formed by the apposition of two furrows in the neighboring surfaces of liver cells, and constitute an extremely fine system of canals which extends throughout the entire parenchyma of the liver. The meshes of this network are decidedly smaller than those formed by the blood capillaries. In general the bile capillaries lie between those cellular surfaces which are not touched by the blood capillaries. Thus the blood capillary and the bile capillary networks do not come into contact. Like the blood capillaries, the bile capillaries as a rule form anastomoses, but in addition there are free, blind, capillary ends which may be either intercellular or intracellular. The latter are found in highly variable numbers as short projections extending into the cell body and terminating in knoblike swellings. They probably have the power of occasionally disappearing and again forming anew.

It may be considered that two neighboring rows of liver cells, along with the bile capillary lying between them, correspond to an earlier (membraneless) liver tubule, the two rows of liver cells representing the wall of the tubule and the bile capillary the greatly reduced lumen. While the lumina of the hepatic tubules, at least in adult man, are usually formed by only two rows of cells, in many animals a bile capillary is bounded by more than two rows of cells; in which case the hepatic tubule resembles that of an ordinary tubular gland. However in the human liver each row of cells belongs at the same time to two or more tubules; since as a rule a liver cell has a bile capillary on each surface which is in contact with other liver cells. According to this conception, each hepatic lobule consists originally of a number of tubules devoid of basal membranes and arranged radially about the axis of the lobule.

The liver also differs in another respect from other glands. The liver cords which correspond to the tubules of other glands do not end blindly but form a network (reticular gland). Moreover the excretory ducts do not enter into the lobules, but begin outside of the latter in the interlobular connective tissue.

Bile capillaries constitute the radicles of the **duct system** of the liver. At the periphery of the lobule these capillaries discharge into the interlobular bile ducts, *ductus biliferi*, which run in company with the interlobular veins and the small arterial branches. The cubical epithelium of the interlobular bile ducts is directly continuous with the cells of the hepatic cords; for neighboring cords unite at the periphery of the lobule to form the wall of the bile duct. In doing so the hepatic cells diminish in size and are transformed into the epithelial cells of the bile duct. Numerous netlike anastomoses of the smaller bile ducts result from this process. The interlobular bile ducts of larger diameter have a columnar epithelium and a fibro-elastic wall (tunica propria) as well as a basal membrane which usually is also present even in the ducts of smallest diameter. The anastomoses cease with the increase in diameter of the ducts. The three large bile ducts (ductus cysticus, hepaticus, and choledochus) have also the same structure as the above; although a few circularly arranged fibers of smooth muscle appear, and short, tubular, mucous glands run a tortuous course in the tunica propria. A more marked accumulation of smooth muscle, with a sphincter-like action, is to be found in the wall of the ductus choledochus close to its termination in the duodenum.

Pl. 51, Fig. 1

Fig. 29

The blood vessels of the liver have already been described. The LYMPHATIC VESSELS accompany the branches of the portal vein and appear also to enter the interior of the lobules, where blood and lymphatic vessels are said to be in direct contact. According to other views perivascular lymphatic sheaths are present. A superficial lymphatic plexus lies close beneath the capsule of the liver. The NERVES of the liver consist chiefly of nonmedullated fibers. They enter at the porta of the liver and follow the course of the branches of the hepatic artery or of the portal vein as the case may be, and consequently also the branches of the bile ducts. They form plexuses in which nerve cells are present. The greater number are vaso-motor nerves, yet secretory nerves extend as far as the liver cells. Certain nerves seem even to enter the liver cells and terminate in networks.

The Gall Bladder, *vesica fellea*

The gall bladder must be considered as belonging to the system of the excretory ducts of the liver and its wall shows a structure similar to that of the larger bile ducts;

Pl. 51, Figs. 3, 4

however, its columnar epithelium differs in being especially thick, in secreting mucus, and in apparently being provided with a cuticular border. It covers the folds of the mucous membrane and lines the crypts which are of variable, and often of considerable, depth. A dense collection of basophilic mucin granules close beneath the surface of the epithelium of the gall bladder and of the larger bile ducts produces the appearance of a cuticular border. Beneath the epithelium there follows a tunica propria, rich in elastic fibers, and a quite strong *tunica muscularis* formed chiefly of bundles which have a circular direction. Towards the neck of the gall bladder there appear tubulo-alveolar mucous glands, while in the remaining parts of the bladder-wall they may be entirely lacking. Where the gall bladder is covered by the peritoneum there is, in addition, a serous coat and subserous tissue which in places is very dense and fibrous.

10. The Pancreas, *pancreas*

In its structure the PANCREAS is closely related to the salivary glands but differs
Pl. 54 from them materially in several of its characteristics. Its terminal secreting parts are
Pl. 53, Fig. 6 essentially[1] of tubulo-alveolar form and in the main resemble those of the parotid gland; for their membrana propria encloses serous cells only, which however are easily distinguished from cells of the parotid gland by the marked difference between their inner and outer zones. The cells, previous to secreting, show near the lumen distinct oxyphilic zymogen granules of considerable size (almost 1 μ). These form a granular inner zone while the basal part of the cell contains no granules and thus constitutes a homogeneous
Pl. 53, Fig. 6 outer zone in which lies the small rounded nucleus. This zone shows fine radial striations, more distinct than those of the cells of salivary glands. During digestion the granules of the inner zone gradually disappear. In proportion as the granules increase in number the nucleus becomes driven towards the base of the cell. In form the pancreatic cells are low-columnar or conical. As in the parotid gland, intercellular secretion canaliculi are present between the cells. Within the cells fine fat (lipoid) droplets may be demonstrated and also a reticular apparatus (p. 5). The secreting parts contain very narrow lumina of characteristic appearance. Frequently the lumen can scarcely be seen, since for a consider-
Pl. 54, Figs. 5, 6 able distance it is filled with flat cells, so-called CENTRO-ACINAR (or centro-alveolar) CELLS.
Pl. 53, Fig. 6 These cells really are a continuation of the flat cells which form the LONG, NARROW INTERMEDIATE DUCTS of the pancreas and which are continued for some distance into the lumen of the secreting part.[2]

The duct system of the pancreas is much less complicated than that of most salivary glands. Secretory ducts such as occur in the latter are entirely wanting. The intermediate ducts pass directly into the branches of the main excretory duct, the ductus pancreaticus. Certain intermediate ducts are similarly related to the ductus pancreaticus accessorius.[3] In both cases the branches unite at acute angles and run almost straight courses for long distances in the gland. As in the salivary glands, there are intermediate ducts of different orders.

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[1] Along with tubulo-alveolar secreting parts there occur others which are almost purely tubular. Branched and twisted tubules with lateral hemispherical enlargements predominate. As probably in all glands, there is here quite a broad gradation of form.

[2] Thus the centro-acinar cells do not at their peripheral ends become continuous with the epithelium of the secreting part. In contrast to the behavior of the epithelium of the intermediate ducts in the salivary glands, these cells lie on the inner surfaces of the glandular cells. However, the centro-acinar cells do not fill the lumen in its whole extent; consequently in sections of the organ very narrow lumina are found entirely free from these cells.

[3] See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II.

The wall of the intermediate duct is formed entirely of flat cells; basal cells, such as occur in the intermediate ducts of the salivary glands, are here lacking; neither are basket cells present in the secreting parts. In other points of structure, and as regards diameter, the intermediate ducts of the pancreas resemble those of the salivary glands. They end in slender branches of the excretory ducts which are lined by cubical epithelium. The larger branches bear a simple columnar epithelium which in the two main ducts becomes a columnar epithelium of two layers of cells. The walls of the ducts consist entirely of connective tissue except at their terminations in the duodenum where a few layers of circular muscle are to be found. Pl. 54, Figs. 3, 7 Pl. 54, Figs. 2 –4

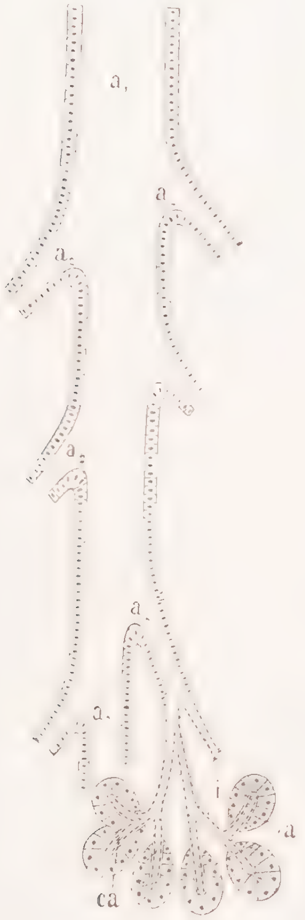

Fig.32. **Diagram of the Structure of the Pancreas**

a_1 = main excretory duct
a_2 = lateral branches
a = tubulo-alveoli
ca = centro-acinar cells
i = intermediate ducts

The greater part of the pancreas shows the structure described above and is thus very intimately related to the serous salivary glands and corresponds to an exocrine gland. On the other hand a small proportion of the substance of the pancreas forms an internal secretion only. This **endocrine** portion of the pancreas is very peculiar since it is not a continuous whole but is subdivided into small island-like areas[1] scattered everywhere throughout the main part of the gland. These are the so-called ISLANDS OF LANGERHANS. They are small masses of approximately spherical or ellipsoidal form, which vary in diameter from 0,05—0,4 mm. and are formed of epithelial cells in cordlike or netlike arrangement with numerous wide capillaries running between the cords. The endocrine cells do not form tubules nor are lumina or secretion canaliculi present. The secretion is taken up directly by the blood capillaries. The islands are sharply marked off from the remaining pancreatic tissue only by their peculiar structure, for as a rule they are not surrounded by a proper connective-tissue sheath.[2] The islands stand in contrast to the larger exocrine mass of the gland, especially in the light quality of the stain taken by their cells which often appear vacuolated. By special methods granules of different kinds may be demonstrated in the cells.

The relations of the blood and lymphatic vessels and of the nerves of the pancreas are the same as they are in the salivary glands. The subdivision of the whole gland into lobules is also similar. Vater-Pacinian corpuscles (p. 181) are to be found with remarkable frequency in the interlobular connective tissue.

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[1] The islands are more numerous in the tail of the pancreas than in the body and still more than in the head of the gland.

[2] Occasionally near the excretory ducts, islands may be found quite isolated in the interlobular connective tissue.

11. The Peritoneum, *peritonaeum*

The peritoneum is a very thin membrane (0.1 mm.) which consists essentially of membraneous connective tissue containing quite large numbers of elastic fibers. A simple squamous epithelium of large, polygonal cells covers the free surface, and rests directly upon a delicate basal membrane. In many areas, particularly within the great omentum, the epithelium is extremely flat and occasionally is even absent. On the other hand at the hilum of the ovary it passes into a cubical epithelium (so-called germinal epithelium,[1] see p. 249) which was its original embryonic type. Occasionally the narrow cement lines become widened into small areas which perhaps come into being through the death of single cells. To these areas the questionable name of stomata has been applied.

Pl. 50, Fig. 4 The fibro-elastic basis is decidedly thicker in the parietal layer than in the visceral layer of the peritoneum. Beneath the connective-tissue serous layer there lies in many regions, but not everywhere, a subserous layer which contains varying amounts of fat, especially in the mesentery; while in the parietal peritoneum it has rather the character of loose connective tissue. Where the subserous layer is lacking (liver, spleen, uterus) the peritoneum is firmly attached to the organ beneath. The peritoneum contains blood vessels, lymphatic vessels and nerves. In general the first named are relatively few; although in certain regions, for instance the great omentum, they are quite numerous. The lymphatic vessels are better developed, and occasionally form rich plexuses, particularly in that part of the peritoneum which covers the diaphragm. It is alleged that certain lymphatic vessels stand in direct connection with the peritoneal cavity by means of openings, the so-called stomata. However their existence, at least in mammals and in man, is more than doubtful, indeed it may be confidently denied. The peritoneal epithelium (not endothelium, see p. 94) as already mentioned, varies greatly from region to region (see ovary, p. 249), and in so doing has great influence upon the character of the peritoneum. This is true, for example for the serous covering of the central tendon of the diaphragm, where the form of the epithelium is somewhat unusual; that is to say, groups of the cells show less flattening than elsewhere, with the result that the epithelium is thicker and the nuclei are placed closer together. This is not the case over the muscular part of the diaphragm where the peritoneum resembles that of the abdominal walls.

The **great omentum,** *omentum majus*, is a part of the peritoneum which has several special peculiarities. Its structure varies considerably at different periods of life; although, of course, it is always composed of the same fundamental constituents as enter into the structure of the peritoneum in general. In addition, there are certain peculiarities lacking in the rest of the peritoneum, such as the so-called milk spots (see below). Apart from the serous epithelium, present here as elsewhere in the peritoneum, the omental substance proper consists of connective tissue rich in cells, which has to a large extent retained its embryonic character. Networks of elastic fibers, particularly of extremely delicate fibers, are abundant in this connective tissue. The cells of the great omentum have in part already been described (p. 64). In this primitive connective tissue there are gaps which in large areas give it an AREOLAR character (p. 64). This omental connective tissue contains numerous blood vessels. In scattered areas there are to be found dense tufts of small blood vessels within which peculiar opaque spots, so-called MILK SPOTS, may be seen. In youth these are produced by dense collections of lymphoid cells so that at first glance the spot would seem to be a small and much flattened lymph nodule. However, no indications of germinal centers are to be found within them.

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[1] In some other situations, *e. g.* in the central tendon of the diaphragm and in the tunica vaginalis propria testis, the epithelium is less flattened than usual.

From these primary milk spots there gradually develop, after early childhood, masses of adipose tissue (see p. 71 for development of adipose tissue from embryonic reticular tissue), which at last completely displace the lymphoid cells. It is noteworthy that under certain conditions these secondary adipose milk spots can again become lymphoid milk spots which in turn may become transformed into fat.

While throughout its whole extent the peritoneum must be described as DECIDEDLY VASCULAR, the number of LYMPHATIC VESSELS is extremely variable. In the great omentum they appear to be entirely absent, while over the central tendon of the diaphragm they are present in unusual abundance.

NERVES are comparatively rare in the visceral layer of the peritoneum, but are abundant in the parietal layer. For the most part they consist of medullated fibers, although non-medullated, vasomotor nerves are also present. Nerve terminations in the form of Vater-Pacinian corpuscles are present in the mesentery and are particularly numerous in the mesentery of the cat.

VI. The Organs of Respiration

1. The Nasal Cavities

We are here concerned only with the structure of the nasal mucous membrane. This is subdivided into three regions: regio vestibularis, regio respiratoria and regio olfactoria. Pl. 55

The **regio vestibularis** is essentially a portion of the external skin and shows all the characteristics of the latter. In particular near the nostrils there still occur stout body-hairs, vibrissae, with large sebaceous glands, also other sebaceous glands which do not accompany hairs. Glands and hairs both cease at a short distance within the nasal cavity; beyond which limit the mucous membrane of the vestibule is distinguished from that of the respiratory region only by the absence of glands and by its stratified squamous epithelium, which however is no longer cornified.

The mucous membrane of the **regio respiratoria,** the main subdivision of the nasal cavity, bears a typical, stratified, ciliated epithelium[1] of several rows of cells (p. 37), which Pl. 55, Figs. 1–3
commonly contains goblet cells and which is separated by a homogeneous basal membrane from a thick layer of tunica propria. The latter, without the intervention of a tunica submucosa, is attached to the periosteum or to the perichondrium as the case may be. The tunica propria contains a few elastic fibers and many cells (see below), among them lymph cells which often give to the nasal mucous membrane the character of a diffuse adenoid tissue and which may even become condensed and form typical solitary nodules. The mucous membrane of the respiratory region contains branched TUBULO-ALVEOLAR GLANDS of mixed character, in which serous cells forming crescents are present along with many mucous cells (p. 194). The mucous membrane is rich in blood vessels, particularly in large veins which in many areas, *e. g.* the posterior portion of the inferior turbinate bone, are so strongly developed as to form a kind of cavernous tissue; their walls are very muscular.

The cellular elements of the nasal tunica propria consist of fibrocytes and colorless blood cells of different types (wandering cells) and also of plasma cells. These cellular Pl. 55, Figs. 2, 3

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[1] The boundary between the ciliated epithelium and the stratified pavement epithelium is variable, the latter often extends beyond the limits of the vestibular region.

Pl. 5, Fig. 2 elements are extremely abundant in the superficial regions of the mucous membrane and are particularly numerous just beneath the epithelium. Deeper in the tunica propria the cells become progressively fewer in number and the fibers more abundant until at last but relatively few fibrocytes are to be found. Thus the tissue of the tunica propria passes gradually into the periosteal or perichondral tissue.

The ACCESSORY CAVITIES of the nose are lined by a relatively thin mucous coat which has a simple ciliated epithelium and few glands or none at all.

Pl. 55, Figs. 4, 5 The mucous membrane of the **regio olfactoria** bears the peculiar non-ciliated olfactory epithelium which will be described in detail in the section on the sense organs. The tunica propria of the regio olfactoria is not so thick as that of the regio respiratoria, nor are the elastic fibers so numerous; cells however are present in large numbers. It contains a special type of gland, the *glandulae olfactoriae* of Bowman [1] which are simple tubular glands with few branches and which consist of serous cells only. The blood vessels (veins) are somewhat less abundant than in the respiratory region. Thick bundles of the non-medullated fibers of the olfactory nerve (p. 295) are found in the mucous membrane of this region.

The nasal mucous membrane is exceedingly rich in BLOOD VESSELS. The arteries are relatively small, but the veins are remarkably numerous and large. The latter form extremely dense plexuses which in part lie very near the upper surface of the tunica propria. These are particularly well developed over the turbinate bones and on the inferior turbinate bone assume an almost cavernous character. At the same time these veins possess an extraordinarily strong musculature. The capillaries form three plexuses; one weak and periosteal in position, a second periglandular and very strongly developed; the third is similar but subepithelial.

The radicles of the LYMPHATIC VESSELS of the nasal mucous membrane lie in the tunica propria where they form plexuses. The deeper vessels run in company with the blood-vessels and it is even stated are in direct connection with the subarachnoid space of the brain.

The NERVES of the nose are partly medullated sensory fibers which terminate between the epithelial cells, and partly non-medullated sympathetic or parasympathetic secretory fibers which arise from the sphenopalatine ganglion. (Concerning the olfactory nerve see p. 295.)

2. The Larynx, *larynx*

The mucous membrane of the larynx bears essentially the same variety of epithelium
Pl. 56 as does the respiratory region of the nasal cavity; *i. e.* a stratified ciliated epithelium with
Pl. 57, Fig. 1 very numerous goblet cells; but the epithelium is generally thicker than in the nasal cavity. At the free borders of the vocal cords it always becomes a stratified pavement epithelium with markedly high papillae; similar epithelium is also to be found on the posterior surface of the epiglottis and to a variable extent on still other areas of the aditus laryngis.[2] The tunica propria is extraordinarily rich in elastic fibers which, toward the

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[1] The glands of Bowman differ markedly from the serous glands of the oral cavity. Apart from their tubular form they have strikingly wide lumina. The cells of the glands are cubical and often pigmented. They contain fine granules and becoming flattened form the lining where the necks of the glands lie between the cells of the superficial epithelium.

[2] The boundaries of the two varieties of epithelium are highly variable. Scattered islands of squamous epithelium are found within the area of the ciliated epithelium. The anterior surface of the epiglottis naturally shows the characteristics of the oral mucous membrane.

deeper part, gradually thicken to form an elastic layer, the *membrana elastica laryngis*. A true tunica submucosa is lacking. In places the tunica propria contains numerous lymphocytes, as in the region of the ventriculus laryngis where they may even produce solitary follicles; since where stratified pavement epithelium occurs the tunica propria usually forms papillae.[1] The latter are particularly high at the true vocal cords where they fuse with one another and form parallel longitudinal ridges. In the same regions, for instance on the epiglottis, there occur isolated taste-buds (p. 294). The mucous membrane of the larynx is the seat of numerous glands of the same character as those of the respiratory region of the nasal cavity. In some places they are present in special abundance as on the ventricular folds and in occasional areas of the aditus laryngis.[2] The epiglottis is often perforated by them but in other places, as on the free border of the vocal cords, they may be entirely lacking. At some points in the vocal cords, for instance at the *macula flava* and frequently in the ventricular folds, there is present dense elastic tissue or even elastic cartilage. A true tunica submucosa is lacking in the larynx but the mucous membrane passes gradually into a kind of submucosa of almost pure elastic tissue, and this in turn into the perichondrium of the cartilage.

Pl. 56, Fig. 1, 3

The LARYNGEAL CARTILAGES are in part hyaline (thyreoid, cricoid and the greater part of the arytenoids), and in part elastic (epiglottis, the processus vocalis and apex of the arytenoids, and the small cartilages of the aditus laryngis).[3] The larger cartilages are surrounded by a perichondrium rich in elastic fibers to which the neighboring mucous membrane is intimately connected unless muscle intervenes (see above).

The muscles of the larynx as a whole consist entirely of striated fibers (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II).

BLOOD AND LYMPHATIC VESSELS are abundantly present in the larynx and form three plexuses at different levels, of which the most delicate, a capillary plexus, lies in the most superficial layer of the mucous membrane.

The NERVE PLEXUSES are two in number, a deep and a superficial. Although medullated fibers predominate, many non-medullated fibers and nerve cells are present. The fibers end chiefly either as intra-epithelial terminations in the mucous membrane, or as motor end-plates in the muscle.

3. The Trachea, *trachea*, and the Bronchi, *bronchi*

Pl. 57, Figs. 2, 3

The walls of the trachea and bronchi are not to be distinguished from one another by their microscopic structure; there are also many points in which they exactly resemble the wall of the larynx. Numerous goblet-cells occur in the stratified ciliated epithelium, the tunica propria is rich in elastic elements, the chief plexuses have their meshes elongated longitudinally and lie close under the epithelium. Lymphatic tissue occurs, even to the extent of forming groups of small lymph nodules. Further there are present, as in the larynx, mixed tubulo-alveolar glands of varying size (up to 2 mm.). These are largest and most abundant in the membranous portion, *paries membranaceus*,[1] of the trachea and in the intervals between the cartilages. In the region of the cartilaginous wall proper, *paries cartilagineus*,[1] where the mucous membrane shows its least thickness, the glands are small and few and opposite the middles of the cartilage rings, their thickest parts, the glands are almost entirely lacking. The large glands of the membranous portion are situated partly in the region of the smooth musculature, but many of them lie beyond its limits.

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[1] Although covered by stratified squamous epithelium the posterior surface of the epiglottis shows only very low papillae, or none at all; while very small lymph nodules are to be found here and there.

[2] In particular there lies around the small cuneiform cartilage a dense mass of glands which is present even though the cartilage may be lacking.

[3] The larger cartilages of the larynx always become ossified in later life by an endochondral process such as occurs in the embryonic skeleton. However the bony tissue is soft and relatively poor in salts of calcium.

Only in the region of the membranous wall is the tunica propria of the trachea and bronchi followed by a distinct tunica submucosa; opposite cartilage this layer is completely lacking. The outer layer of the wall is formed partly of hyaline cartilage ($^3/_4$-rings) and partly of smooth muscle and connective tissue. The strands of smooth muscle run for the most part circularly and are attached to the free ends of the rings of cartilage. Elastic fibers are present in the cartilages of the trachea and in still greater number in those of the bronchi.[2]

The cartilage and the muscle are followed by an adventitious layer of connective tissue which is most distinct in the membranous portions where it contains the parts of the glands that lie external to the muscle. Here also there are occasionally found isolated strands of smooth muscle which run longitudinally.

Blood vessels, lymphatics and nerves have the same relations microscopically as in the larynx.

4. The Lung, *pulmo*

Pl. 57, Fig. 4
Pl. 58, Figs. 1—4
The large **bronchial branches** lying within the lung have the same structure as the trachea and the bronchi. In essentials this remains true of the further bronchial branching, but with two exceptions. 1. The cartilages of the bronchi of medium size no longer form half-rings but are anastomosing PLATES distributed irregularly in the bronchial wall. Neither are they now of hyaline cartilage but progressively are becoming purer elastic cartilage. Growing ever thinner they continue until the bronchi have diminished to a
Pl. 58, Figs. 1—3
diameter of about 6 mm. 2. The smooth MUSCULATURE diminishes with the decrease in diameter of the bronchi and may be followed over the borders of the cartilage until, in the finer bronchi, it forms a weak but almost continuous circular layer which lies to the INNER side of the cartilage plates. It may be followed across the cartilage plates into the bronchioles and in part even into the alveolar ducts. Thus the distinction between
Pl. 58, Fig. 1
the paries cartilagineus and the paries membranaceus vanishes. The smooth musculature of the walls of the bronchial branches and of the bronchioles does not form an unbroken sheet as in the intestine but consists of numerous rings of muscle anastomosing at acute angles. The glands of the bronchial wall form a layer which differs from the corresponding layer of the trachea inasmuch as in the smaller bronchial branches it lies in the adventitia external to the cartilage. Otherwise the description, already given, of the tracheal glands holds good for those of the bronchial wall. The intervals between the plates of cartilage are quite filled with glands, while over the crests of the plates the glands are entirely absent.

As already stated the musculature of the bronchial branches in the lungs and of the bronchioles consists of muscular rings which cross and anastomose at acute angles. The distance between these rings of muscle increases as the caliber of the bronchiole diminishes, consequently in the respiratory bronchioles the areas of the wall that are free from muscle are decidedly large and distinct.

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[1] See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II.

[2] For the structure of the tracheal cartilages see p. 75.

The musculature now extends to the alveolar ducts, leaving the walls of the alveoli free, consequently bundles of smooth muscle occur in contact with the alveolar walls only at the mouths of the alveolar openings, and not always there. The extent of the musculature is a matter of considerable individual variation.

Still more variable in different individuals is the presence of smooth muscle in the interstitial connective tissue of the lungs and of the pleura. Occasionally there are found in the interlobular septa whole fenestrated membranes of smooth muscle; while in the perivascular tissue it may appear as scattered strands without any regular arrangement. In the visceral pleura a large quantity of muscle may be present as interwoven strands.

Towards the finer bronchial branches the glands of the mucous membrane become Pl. 57, Fig. 4 few and smaller, but for the most part continue almost to the limits of the cartilage. As Pl. 58, Figs. 2, 3 the bronchial branches progressively diminish in caliber, glands and cartilage cease at about the same point, the glands somewhat earlier. Such small twigs of the bronchial tree, containing neither cartilage nor glands in their walls are known as **bronchioles.** However they still contain smooth muscle and are lined by a simple ciliated epithelium up to their terminal branchings.

In other regards the wall, and in particular the mucous membrane, of the smaller bronchial branches differs but little in structure from that of the larger branches and of the trachea. The essential differences concern the modifications of the epithelium. As far as, or even beyond, the limits of the cartilage the epithelium is ciliated and stratified, or rather many-layered. In the bronchioles which are free from cartilage it consists of one layer only, but retains the cilia although goblet cells no longer are present. The *tunica propria* of the smaller branches contains, close under the epithelium, very strong elastic fibers running in a longitudinal direction. In proportion as the wall of the bronchiole contracts these cause the mucous membrane to project as longitudinal ridges more and more deeply into the lumen, causing the latter to assume a stellate form. As in the mucous membrane of the larger branches, lymphoid tissue is present in the form of solitary follicles. Pl. 58, Fig. 2

As in the case of the trachea, each bronchial branch is surrounded by a TUNICA ADVENTITIA of connective tissue rich in elastic fibers. This adventitia contains the nerves and vessels, and in part the glands. It is also the favorite seat for the deposition of dust.

In contrast to the parts of the bronchial tree described above the **respiratory portion** Pl. 58, Fig. 3 of the lung shows the following structure. The *bronchioli respiratorii* follow the bron- Pl. 59, Fig. 1 chioles and represent direct continuations of the bronchioles of least caliber. In place of a ciliated there is a cubical or flat-cubical epithelium, which changes in the respiratory bronchioles, near the alveolar ducts, into the so-called RESPIRATORY EPITHELIUM, a type of epithelium which in general covers the surfaces of the alveolar ducts and alveoli. It consists of modified, cubical, nucleated cells like those lining the greater part of the respiratory bronchioles and of quite flat, non-nucleated cells of varying but usually large size lying between the others. While in the alveoli and alveolar ducts the flat cells predominate, Pl. 59, Fig. 2 they first appear in the course of the respiratory bronchioles singly or in little groups.[1]

Apart from the epithelium, the walls of the alveoli and of the alveolar ducts consist for the most part of a lightly striated but otherwise structureless basal membrane, and of elastic fibers which commonly show a circular arrangement in the alveolar ducts and form a kind of ring at the entrance to each alveolus. Beyond this the elastic fibers separate and those of neighboring alveoli form the common interalveolar septum.[1] Collagenous tissue is entirely wanting.

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[1] According to one opinion the non-nucleated plates are formed by the fusion of several cubical cells with the loss of their nuclei. According to another, and less probable, opinion they represent only flat processes of the nucleated, cubical cells. The fact that they are separated from the cubical elements by distinct cell-boundaries is against the latter opinion.

While the respiratory bronchioles diminish gradually but markedly in caliber and finally have a diameter of only 0.3 mm. the blind-ending alveolar ducts which proceed from them are of substantially greater caliber; although as in the alveoli themselves the width of the lumen is largely dependent upon the extent to which they are filled with air. In inspiration the diameter of an alveolus measures 0,3 mm. and more; on expiration it measures only 0.1 mm. The diameter of the alveolar duct is almost twice as great; its length is about 2—3 mm.[2]

Single alveoli first appear in the wall of the respiratory bronchiole as lateral evaginations; but the chief mass of them is situated on the walls of the alveolar ducts, the neighboring alveoli being so closely pressed together as to have a common wall, the interalveolar septum.

The alveoli and alveolar ducts of the lung together represent the parenchyma of the organ which must be considered as a true gland, not merely in development but also in its structure. In the next place a certain number of alveolar ducts along with their alveoli form a pulmonary lobule, **lobulus pulmonis.** The alveoli and alveolar ducts are pressed closely together along with the bronchiole from which the alveolar ducts proceed, the whole having an average diameter of about 1 cm.[3] A bronchiole of larger diameter conducts the air to the lobule within which it divides into correspondingly smaller branches, bronchioli intralobulares, these in turn divide into respiratory bronchioles from which the alveolar ducts proceed. Within the pulmonary lobule, but only in the immediate neighborhood of the bronchiole, there is a small amount of connective tissue which accompanies the nerves and the fine branches of the vessels nourishing the parts; otherwise the lobule consists only of the alveolar walls whose structure has been set forth above.

The individual pulmonary lobules are separated by connective tissue, the so-called INTERLOBULAR TISSUE, which in man is small in amount but rich in elastic fibers. Beside vessels and nerves it usually contains in the lung of adult civilized man pigmented deposites consisting of dust withdrawn from the inspired air through phagocytic activity.

This **pigment** usually is pure coal-dust (so-called anthracotic pigment) which, in spite
Pl. 57. Fig. 4 of the purifying action of the ciliary current of the epithelium lining the respiratory passages, has reached the alveoli with the inspired air. Naturally it cannot remain there long lest it interfere greatly with the exchange of gases in the lungs. It is not altogether certain which cells may be the first phagocytes, but it appears that beside the wandering cells to which naturally belongs the chief role in the transport proper, the alveolar epithelium itself is capable of phagocytic activity. The foreign matter, whether dust of coal or of other materials, is carried away from the alveoli by wandering cells and by colorless blood cells drawn to the locality by the irritation of its presence. These cells then either settle in the interlobular tissue and die there so that only the coal-dust remains, or they

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[1] These septa have fine openings by which neighboring alveoli stand in communication with one another. In many animals they are more numerous and regular than in the human lung, in which however they are not lacking.

[2] Two quite superfluous terms, infundibulum and atrium, have both been used to designate the transition from the respiratory bronchiole to the alveolar duct, and also the blind end of the latter.

[3] The size of the lobule varies; it is also naturally dependent upon the degree of distention by the air in the alveoli and alveolar ducts.

work their way along in the peribronchial connective tissue where they meet the same fate and form anthracotic pigment; or by way of the lymph stream they reach the lymph glands of the region and there die in increasing numbers,[1] depositing the phagocytosed foreign matter. The lymph glands concerned become more and more intensely black and in time are destroyed; in their place appear hard, black masses which formerly were lymph glands but now consist only of accumulations of coal-dust. Naturally the process is similar when other foreign material in dustlike form gains admittance into the alveoli. Dust is also deposited in the sub-pleural connective tissue.

The **blood vessels** of the lung are primarily those of the pulmonary circulation. Branches of the arteria pulmonalis enter the lung at its hilum and ramify in company with the bronchial branches within the organ. The finer branches enter with the bronchioles into the individual lobules where they break up into an extremely fine-meshed net of very wide capillaries, the finest capillary network in the body, the meshes of which are so small that the area between the anastomosing capillaries is often less than the surface covered by the capillaries themselves. The capillary networks lie almost bare in the alveolar septa, surrounded only by a few elastic fibers (p. 225); as a result they are in immediate contact with the respiratory epithelium.

Pl. 58, Fig. 4

The arteries of the lung carry "venous" blood which after passing through the capillary circulation is returned to the heart by the pulmonary veins,[2] rich in oxygen and poor in carbon dioxide. The course of the veins is separated by a slight distance from that of the arteries, and in consequence also from that of the bronchial branches.

Beside the pulmonary circulation there are also in the lung the *arteriae bronchiales*,[2] arteries belonging to the systemic circulation and carrying arterial blood. They are practically confined to the walls of the bronchi where their capillaries pass into veins. Anastomoses occur between the two circulations in so far as the smaller bronchial veins empty into the pulmonary veins; only the capillaries of the wall of the medium and large bronchi produce bronchial veins proper.

The radicles of the **lymphatic vessels** of the lung are not sufficiently well known, in particular it is as yet uncertain whether lymphatic capillaries occur in the alveolar septa. There is a wide-meshed plexus in the interlobular connective tissue, and the bronchial walls contain lymphatic vessels. A superficial plexus with very fine meshes and occasionally small lymph nodules lies beneath the pleura.

In addition, until the bronchioles are reached, the peribronchial connective tissue always contains an abundance of lymphatic or adenoid tissue which may form complex masses, especially at the division points of the bronchi. In the adult, lymph nodules with germinal centers are rarely to be found in this lymphatic tissue of the deeper parts of the lung; but in the child's lung there often occur here true lymph glands of small size, such as are in later life to be found as a rule only near the hilum.

Pl. 58, Fig. 2

The **nerves of the lung** arise partly from the nervus vagus, partly from the sympathetic system. Isolated nerve cells are present and both medullated and non-medullated nerve fibers; the latter go to the blood vessels, to the musculature of the bronchi and perhaps also to the mucous membrane. Whether the medullated fibers reach the alveolar wall or end in the alveolar septa is unknown.

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[1] A number of the dust-laden wandering cells die before reaching the lymph glands and set their dust free in the lymph. It is then phagocytosed by the reticulo-endothelial cells of the lymph gland (p. 95) and is thus rendered innocuous.

[2] See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II.

5. The Pleura, *pleura*

The pleura resembles the peritoneum (p. 220) in the essentials of its structure; here also the rule holds good that the parietal layer shall be decidedly thicker than the visceral. Pl. 59, Fig. 3 The latter shows one peculiarity of structure not present in the peritoneum; it contains an abundance of smooth muscle, often in quite large masses, whose individual bundles may form a network.

Appendages of the Respiratory Tract

1. The Thyreoid Gland, *glandula thyreoidea*

The thyreoid gland will be discussed here although it is an appendage of the respiratory tract only in a topographical sense. Pl. 59, Figs. 4, 5 Pl. 60, Fig. 1 In its fully developed form it is a typical ductless gland, with an internal secretion. It originally possessed a duct, the ductus thyreoglossus, by which it stood in connection with the oral cavity,[1] but later the duct became obliterated and left the gland to consist only of secreting alveoli. The thyreoid gland consequently belongs to the first type of the glands with internal secretion (p. 47).

The follicles or alveoli of the thyreoid gland, although somewhat irregular, are approximately spherical; Pl. 59, Fig. 4 Pl. 60, Fig. 1 occasionally irregularly ellipsoidal forms are found and others which show indications of branching. The diameter of the lumen is highly variable; usually it measures from 50—150 μ, but occasionally it may be much larger. The follicles are lined by a single layer of epithelial cells which usually are cubical, but in rare cases may be either low-columnar or even flat. The epithelium rests immediately upon the scanty connective tissue (see below) which separates the follicles. There is thus no membrana propria.

The division of the epithelium into two types of cells, chief cells, and colloid cells, Pl. 59, Fig. 5 is quite artificial. They are the same type of cell in different stages of secretion, the so-called colloid cells probably representing a stage of exhaustion.

Like the cells of other glands those of the thyreoid body contain various cell inclusions such as reticular apparatus, chondricontes and centrosomes. In their superficial zones they also show fine, highly refractive, lipoid granules.

In addition to the epithelium which forms the walls of the follicles there are always present masses of so-called interfollicular epithelium, *i. e.* groups of epithelial cells which do not surround a lumen and which are probably in a (temporarily?) functionless condition.

Within the follicles there is always found a greater or less amount of the secreted material, the so-called COLLOID. This is a vitreous substance of high refractive index which has been quite erroneously named. In the centre of the mass of colloid, which stains intensely with acid aniline dyes, vacuoles are frequently present; in addition the colloid often appears retracted in scallops from the walls. Whether the vacuoles contain a mucoid material is doubtful.

A variable number of follicles, bound together by a small quantity of interstitial connective tissue, form a lobule, *lobulus glandulae thyreoideae*. The connective tissue contains the larger blood vessels and accompanies the very numerous capillary branches into the interior of the lobule between the follicles.

The thyreoid gland is exceptionally rich in BLOOD VESSELS. In proportion to its bulk the organ receives on an average about fifteen times as much blood as the other organs of the body. The capillaries surround the follicles with a dense network[1] and the lymphatic vessels are equally abundant, surrounding the follicles in deep plexuses which may be distinguished from the more superficial plexuses. There are no connections whatever between the lymphatic vessels and the cavities within the follicles, although for a long time the existence of such connections was accepted.

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[1] See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II.

The majority of the NERVE FIBERS of the thyreoid gland are of the non-medullated variety. They are partly vaso-motor and partly secretory nerves. The latter reach the cells of the follicle where they terminate simply against the basal surfaces of the cells.

2. Parathyreoid Glands, *glandulae parathyreoideae*

ACCESSORY THYREOID GLANDS *(glandulae thyreoideae accessoriae)* have a structure similar to that of the principal gland, but the "*glandulae parathyreoideae*" which are constantly present on the posterior surface of the gland, and which are usually four in number,[2] have a quite different structure. They belong to the so-called epithelial corpuscle type of gland, *i. e.* they are irregular masses of epithelium which neither form tubules nor enclose lumina, but which are surrounded by connective tissue containing numerous capillaries.

Pl. 60, Fig. 2

As regards the finer structure of the parathyreoid gland there may be recognized a thin connective-tissue capsule which contains a few elastic fibers. This capsule sends into the gland processes or septa which cause a more or less complete subdivision of the gland into masses of epithelium. The greater part of the epithelium is formed of a single type of cell, the so-called chief cell. This is a small cell (4—7 μ), with few peculiarities[3] and a characteristically slight affinity for stains. The chief cells usually form compact masses or chains, but quite exceptionally they surround a small cavity filled with colloid matter. Scattered among them singly or in small groups there occur larger (ca. 15 μ) oxyphilic cells.

Pl. 60, Fig. 2

VII. The Urinary Organs

1. The Kidneys, *renes*

The kidney is a large, compound tubular gland whose excretory duct is the *ureter*. However the latter and its radicles, the renal pelvis and the calyces, are not considered as parts of the kidney in the narrower sense.[4]

Pl. 59, Fig. 6
Pl. 60, Figs. 3, 4

The **renal parenchyma** is formed of the **renal tubules,** *tubuli renis*; these are slender tubules of considerable length which end blindly and which differ greatly in shape in different parts of their course. A large number of these tubules join to form a duct of large diameter, the ductus papillaris; about twelve such ducts open upon the apices of each renal papilla.

Pls. 61, 62

Each renal tubule consists of an apparently structureless (see below) membrana propria and a simple epithelium. The diameter of the tubule, the thickness of its wall, the height and characteristics of the epithelium, all undergo considerable variations in different parts of the tubule. In particular the secreting portion next to the blind end of the tubule is decidedly different in structure from the ductlike portions. The former constitutes essentially the *pars convoluta* of the renal cortex *(substantia corticalis)*; while the latter forms the *pars recta* of the cortex and medulla *(substantia medullaris)*.

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[1] The small arteries of the thyreoid gland display regular thickenings of the intima which appear as bud-like projections into the lumen (so-called buds of Schmidt). They are perhaps consequences of thickenings of the musculature. The points where arteries divide are especially favored in the occurrence of these buds.

[2] See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II.

[3] However, by the use of special methods, granules may be demonstrated in these cells.

[4] In their development, the ureter, pelvis, calyces and medulla of the kidney form a single group.

Fig. 33 The RENAL TUBULE begins with the renal corpuscle, *corpusculum renis* (of Malpighi), which is followed by the convoluted part of the tubule, *pars convoluta* (tubulus contortus), which generally lies peripherally from the Malpighian corpuscle. The convoluted part of the tubule is joined to two straight parts which together form the portion known as the LOOP OF HENLE. This so-called loop is peculiar in consisting of two straight, parallel, and rather narrow portions of the tubule which lie close together and run more or less deeply into the medulla. One part, the proximal limb, runs downward from the convoluted tubule; the other, the distal limb, retraces this course from the medulla upward into the cortex. The point at which the one limb passes into the other, the BEND OF THE LOOP, lies in the medulla. The proximal, DESCENDING LIMB is, for the most part, thinner than the distal, ASCENDING LIMB. In the longer loops of Henle, which in man are much more rare than are the shorter, this relation is quite clear in the greater part of the loop, although the thin portion extends beyond the bend of the loop and encroaches on the lower part of the distal limb; while at the same time the convoluted tubule continues its structure for a distance into the upper part of the proximal limb. On the other hand in the shorter loops the thin portion is usually quite short and the bend of the loop is formed of the thicker part which, gradually changing the character of its epithelium, passes into the distal convoluted tubule. This DISTAL CONVOLUTED PART follows the loop of Henle, is distinctly convoluted and lies in the pars convoluta of the renal cortex intimately associated with the windings of the proximal convoluted part of the tubule. The distal convoluted part is inserted between the secreting portion of the renal tubule and the so-called collecting tubules which begin the duct system. These collecting parts are straight tubules which join at acute angles, increasing progressively in diameter. Their proximal parts form the *pars radiata* of the medulla while their terminal portions are represented by the ductus papillares.

Fig. 33 The blind end of the renal tubule is formed by the **renal corpuscle** (of Malpighi),
Pl. 61, Fig. 2 *corpusculum renis*. It has a diameter of 0.13—0.22 mm., is approximately spherical and
Pl. 60, Fig. 4 consists of two quite different parts, one of which is an arterial rete mirabile, the *glomerulus renis*, and the second is the glomerular capsule, *capsula glomeruli* (of Bowman). Only the latter is really the blind end of the renal tubule; it forms a spherical or sac-like structure into which the glomerulus is invaginated. Because of this invagination it is possible to distinguish in the glomerular capsule two lamellae separated by a narrow cleft. One, the inner, is applied to the capillary loops of the glomerulus and may be termed the VISCERAL layer, by analogy to the layer of the peritoneum which is similarly related to the viscera. This layer follows all the irregularities and enters all the depressions of the surface of the glomerulus. The external or PARIETAL lamella has almost exactly the form of a smooth, hollow sphere. The two lamellae join at the point where the glomerulus is invaginated, the so-called neck of the glomerulus; there is no boundary line between them, but they differ in structure. The visceral layer, at least in the adult condition,[1]

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[1] In young animals instead of an extremely flat syncytium this layer is marked off into cubical cells. According to a view different from that given above the cells have boundaries in the adult, but are branched.

is a thin syncytium with flat nuclei but without cell boundaries. On the other hand the parietal layer is formed of flat, polygonal, clearly defined cells which rest upon a delicate, structureless basal membrane (see below). Opposite the neck of the glomerulus the outer layer passes by a more or less sharp transition into the epithelium of the proximal convoluted tubule.

The **proximal convoluted part** of the renal tubule, *tubulus renalis contortus* (pars convoluta tubuli renalis) is the first part of the truly tubular portion of the renal tubule. It has a considerable diameter (40—55 μ) and arises more or less abruptly from the parietal wall of the glomerular capsule, the epithelium rapidly becoming low columnar or cubical. Usually the lumen is but moderately wide, its diameter varying from 15—25 μ according to the stage of secretion.[1] In the fresh condition the epithelium itself appears dark and opaque. In fixed preparations it is finely granular, strongly oxyphilic and shows two characteristic peculiarities, a coarsely STRIATED BASAL PORTION and a strongly marked BRUSH BORDER. The former is most clear in the basal half of the cell and resembles the corresponding striation in the epithelium of the salivary ducts. Under moderate magnification the appearance is that of striation, but under higher magnification it is seen to consist of protoplasmic granules (plastosomes? see pages 5 and 42) arranged in radial rows.

Pl. 61, Figs. 1—3

The BRUSH BORDER covers the free surfaces of the cells and appears as short, rigid fibrils of protoplasm that look like cilia. Probably its height varies according to the stage of secretion. The boundaries of the individual epithelial cells of the proximal convoluted part of the tubule are so poorly marked that in perpendicular section the impression is given that the epithelium is a syncytium.[2] The nuclei are usually quite spherical and lie close to the centers of the cells.

Pl. 61, Fig. 3

The portion of the proximal limb of the loop of Henle which is adjacent to the convoluted tubule shows the same structure as that described above and consequently is often regarded as part of the latter. This portion is followed by a sudden narrowing of the tubule to a diameter of from 9—16 μ which marks the beginning of the descending part of the true **loop of Henle.** This thin portion of the loop is of highly variable length[3] and consists of very flat epithelial cells surrounding a lumen which is relatively wide in proportion to the diameter of the tubule. The cells are clear, stain poorly with acid aniline dyes and have nuclei which are but moderately flattened and which consequently bulge into the lumen. The thicker limb of the loop of Henle which arises from the pale, thinner limb by a sudden increase in diameter (25—28 μ), as a rule forms the greater part of the distal limb and resembles in structure the proximal convoluted part of the tubule. However its cells, although dark and opaque, are decidedly shorter than those of the convoluted part. In addition, the basal striation and the brush border are never present, nor is the granular protoplasm so strongly oxyphilic. Distinct cell boundaries and terminal bars are visible. The lumen of this part of the loop, although usually narrower than that of the slender part, may occasionally be wider. The succeeding portion of the distal limb passes into

Pl. 61, Figs. 4—7

Pl. 61, Fig. 4

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[1] The height of the epithelium naturally varies with the width of the lumen and the stage of secretion. In the interior of the lumen of the proximal convoluted tubule are found pale, spherical, vesicular droplets of secretion (artefacts?).

[2] That the cells have boundaries is shown best by the possibility of demonstrating terminal bars in the epithelium. The outlines of the cells are extremely zigzag, consequently they are difficult to see. The cells are in contact by grooved surfaces.

[3] Occasionally in man it may be entirely absent.

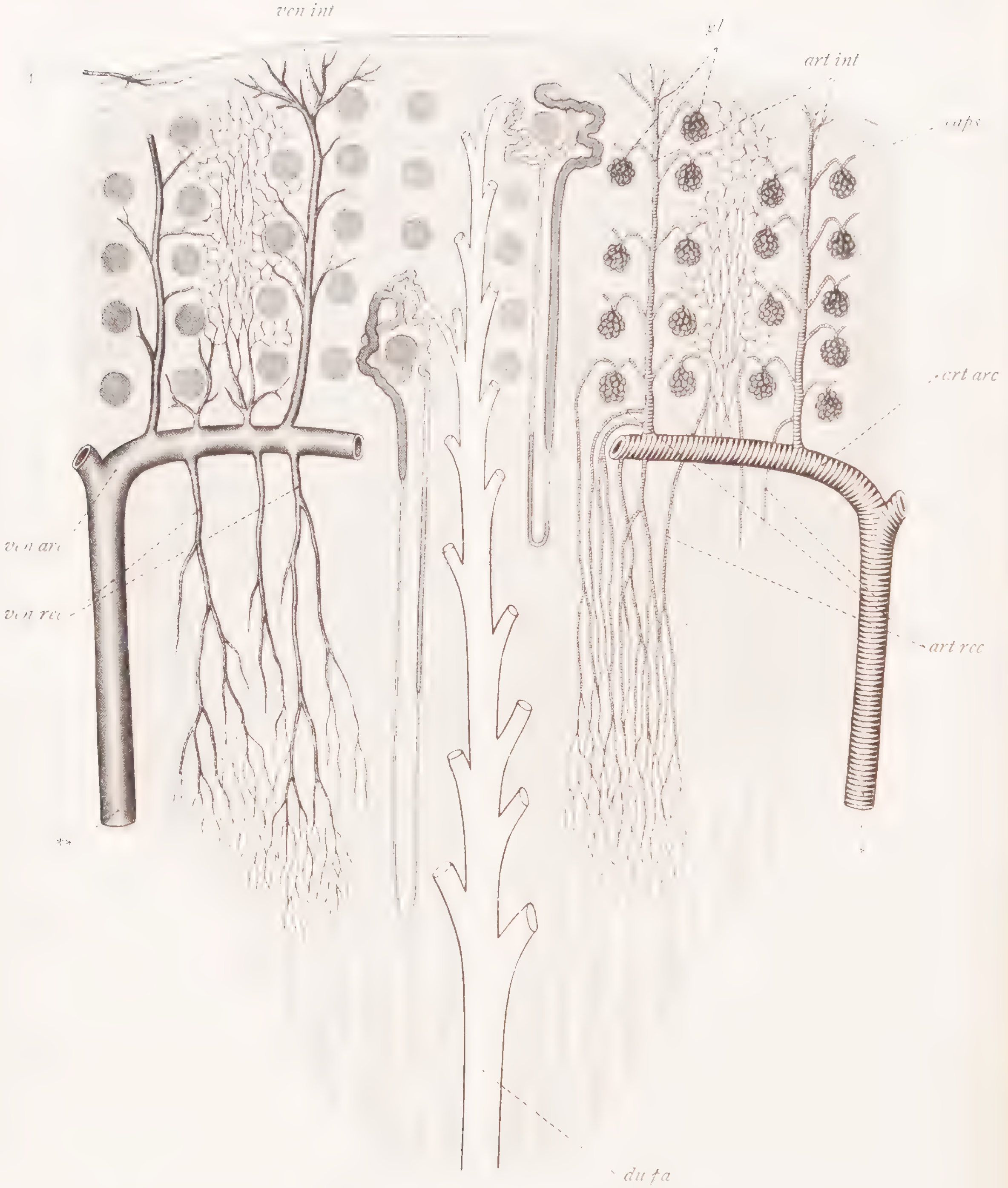
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Fig. 33. **Diagram of the Structure of the Kidney.**

In the center there is represented a papillary duct receiving the terminations of collecting tubules. Two renal tubules are figured in their entire length; in the pars radiata of the cortex they are seen to pass the distal convoluted part of the tubule and is formed of epithelial cells which are much clearer and less granular (see below).

The **distal convoluted part** of the tubule succeeds the loop of Henle. In diameter it Pl. 61, Figs. 1, 2
measures about 40 μ. It lies in the cortex in the immediate neighborhood of the proximal convoluted tubule but is easily distinguished from the dark loops of the latter by the strikingly clear appearance of its epithelium. Its protoplasm is not strongly oxyphilic as is that of the proximal convoluted tubule, but stains quite poorly with acid aniline dyes and contains extremely fine granules which disappear near the collecting tubule. The cells have no brush border or basal striation. The lumen of the distal convoluted tubule is, in general, larger than that of the proximal convoluted part and consequently the epithelium is lower. Just as the structure of the proximal convoluted part of the tubule extends for a distance into the loop of Henle, so the structure of the distal convoluted tubule begins in the upper part of the distal limb of the loop.

As the **collecting tubules** in their course receive the distal convoluted parts of the Pl. 61, Fig. 7
renal tubules their diameter gradually increases from 25 or 30 μ to 250 μ. The smaller branches of the collecting tubules have a cubical epithelium which later becomes columnar and in the papillary ducts is a high columnar epithelium without any peculiarities. The cell boundaries are clearly marked and the cytoplasm is very slightly oxyphilic.

While the renal tubules form the greater part of the renal parenchyma, naturally **interstitial** connective **tissue** is also present. However it is extremely scanty, particularly in the cortex; consequently the kidney, like the human liver, is an organ very poor in connective tissue. Externally the kidney is covered by a rather dense capsule of connective tissue, the *tunica fibrosa renis*, containing a very few elastic fibers and, in its deeper layers, scattered fibers of smooth muscle.

The interstitial connective tissue is extremely scanty in the cortex of the kidney. Pl. 59, Fig. 6
Preparations made with ordinary stains give the impression that the basal membranes of the tubules are in direct contact. Actually between the membranes there are to be found only reticulum fibers such as form the membranes themselves (p. 61). As a result there is only a slight connection between the renal capsule of collagenous fibers and this reticular tissue; hence the ease with which the capsule may be stripped off the kidney. Besides being present in the capsule of the kidney true collagenous tissue occurs only around the larger vessels which enter or leave the renal substance. For even the connective tissue of the medulla, which is much more abundant than that of the cortex, is a primitive tissue containing relatively few fibers and recalls gelatinous connective tissue rather than the Pl. 60, Fig. 3
fully developed collagenous variety.

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into two primary collecting tubules. Of the renal tubules which are represented the one on the left shows a long loop of Henle while the loop on the right is of the short variety. On the right and on the left the relations of the blood vessels are represented, arteries on the right, veins on the left and capillaries on both sides. Two interlobular arteries and veins are to be seen, as well as arteriolae and venulae rectae.

art arc = arteriae arciformes
art int = arteriae interlobulares
art rec = arteriolae rectae
caps = renal capsule
du pa = ductus papillaris
gl = glomeruli

ven arc = venae arciformes
ven int = venae interlobulares
ven rec = venae rectae
* = large branch of renal artery
** = large radicle of renal vein
+ = anastomotic branch to the renal capsule

Fig. 33 Pl. 62, Fig. 1 The **blood vessels** of the kidney show an arrangement which is very characteristic of the organ. The ARTERIES with their chief branches enter the renal substance from the sides of the pyramids at the boundaries of the renal columns (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II). Without branching they reach the level of the boundary between cortex and medulla. Here the chief trunks of the renal artery branch into the so-called *arteriae arciformes* which run arcuate courses (so-called pseudo-arcades) at the boundary between cortex and medulla. From the convex side of the arch, next to the cortex, there arise the chief branches, the *arteriae interlobulares*,[1] for the supply of the CORTEX. These enter the pars convoluta and give off the *arteriae afferentes* (vasa afferentia) to the glomeruli of the renal corpuscles; while the end of the interlobular artery breaks up into capillaries for the renal capsule and the substance of the cortex. In addition there arise from the arcuate arteries the arteriolae rectae (see below). However the existence of these arteries has recently been disputed (arteriolae rectae spuriae).

Pl. 62, Fig. 2 The *glomerulus* is in reality an arterial rete mirabile, that is to say, a network formed by an artery which breaks into anastomosing branches which again unite to form a single artery. Both the afferent vessel, vas (or better arteriola) afferens and the smaller efferent vessel, vas (or arteriola) efferens, are arteries. The vascular loops of the glomerulus are wider than usual and show the structure of capillaries; their walls consist of an endothelial syncytium without cell boundaries. The true capillaries are derived from the vasa efferentia of the glomerulus and supply in part the cortex, both pars radiata and pars convoluta. In addition there are tiny arteries, arteriolae rectae (verae), which run straight courses extending into the medulla.

Pl. 62, Fig. 3 The VEINS of the renal cortex arise as *venulae stellatae* (the stellulae Verheynii of older anatomy) from the union of a number of capillaries and smaller veins, lying in the cortex immediately beneath the capsule. Their direct continuations form the *venae interlobulares* which receive the blood from capillaries in the deeper parts of the cortex. The interlobular veins accompany the arteries closely and join the arcuate veins which in position and relations fully correspond to the arcuate arteries.

Pl. 61, Fig. 3 Fig. 33 Pl. 62, Fig. 1 While the renal cortex is very rich in blood vessels the vascularization of the MEDULLA is much less profuse. Since the main branches of the renal vessels follow the boundary between cortex and medulla the latter contains no large vessels of its own but is provided only with relatively small, recurrent vessels from the cortex. The larger arteries and veins of the medulla are termed arteriolae and venulae rectae because of their straight courses, parallel to the courses of the collecting tubules. The capillaries form networks with much elongated meshes. The arteries of the medulla are partly (but it would seem rarely) direct branches from the concavity of the arcuate arteries; but more frequently they are the vasa efferentia from the deeper glomeruli, or are deep, direct branches from the interlobular arteries. Accordingly arteriolae rectae verae are to be distinguished from arteriolae rectae spuriae. Small numbers of these arteriolae rectae lie close together forming a group. The venulae rectae have a similar arrangement and usually terminate directly in the arcuate veins. While the arteries of the kidney are definitely terminal arteries, in some places anastomoses occur between the smaller arteries and veins. A few small blood vessels in the immediate neighborhood of the kidney enter the renal capsule; but these are not branches of the renal vessels, nor except in rare cases do they anastomose with them.

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[1] So-called because all the renal tubules belonging to a single papillary duct are considered to form a renal lobule. However the renal lobules are not marked off from one another.

The **lymphatic vessels** of the kidney have in part the same course as the blood vessels and are derived from a plexus of lymphatic capillaries in the cortex[1] or in the medulla. However some of the lymphatic capillaries of the cortex pass into a superficial, coarse lymphatic plexus in the capsule. Larger lymphatics run with the interlobular arteries and veins, forming plexuses and finally passing into the large trunks which wind between the pyramids.

The numerous **nerves** of the kidney are chiefly of the non-medullated, sympathetic variety and accompany the arteries, around which, especially in the renal sinus, they form plexuses containing nerve cells. Their terminal branches surround the renal tubules and pass between the epithelial cells to form simple intra-epithelial terminations.

2. The Ducts of the Kidney

To the duct system of the kidney belong the RENAL CALYCES and the RENAL PELVIS, Pl. 63 the URETER, and URINARY BLADDER, the FEMALE URETHRA and the FIRST PORTION OF THE MALE URETHRA. All these are distinguished by being lined with the same type of epithelium, the so-called TRANSITIONAL EPITHELIUM (p. 36), which is confined to the regions named.

This epithelium shows a somewhat greater thickness in the bladder than in the ureter Fig. 4 and renal pelvis; but on the whole has a similar structure in all the subdivisions of the urinary tract. All these parts, particularly the bladder, are capable of great distension. When distended, as when the bladder is full, the epithelium is low and occasionally in extreme distension shows but two layers. In the opposite condition, when the bladder is empty, the number of layers becomes much increased.[2] When the bladder is distended the epithelium is often only one fourth as thick as when the organ is undistended. The cells of the superficial layer are polygonal, often contain several nuclei and according to Pl. 3, Fig. 5 the degree of distension are flat, or cubical, or even columnar. On their surface is a dense exoplasm which may be distinguished from a paler, deeper endoplasm. The deeper surfaces of these cells have from one to several depressions which lodge the upper ends of the cells beneath. In the contracted condition the latter cells are quite long and have markedly alternating nuclei, while the deeper cells are again shorter. The transitional epithelium does not rest on a basal membrane. As a result there may be found, particularly in the renal pelvis and in the ureter, so-called intra-epithelial capillaries. These are capillaries from the most superficial part of the tunica propria, some of whose elements, (fibrils and single cells) accompany them deeply into the epithelium; consequently in oblique and tangential sections the capillaries appear to lie within the epithelium.

No peculiarities are to be seen in the mucous coat of the radicles of the ureter *i. e.* of the *calyces renales* and *pelvis renalis*, nor in that of the ureter itself, which shows marked Pl. 63, Figs. 1–3 folds in the empty condition. The tunica propria is a thin layer of connective tissue containing a few elastic fibers and passing without sharp boundary into the looser submucous tissue. A true, well-defined "submucosa" consequently does not exist in the parts above mentioned. Glands are entirely absent nor is there a tunica muscularis mucosae. On the other hand the mucous coat contains quite numerous lymph cells which occasionally show marked aggregations and are even to be found migrating into the epithelium.

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[1] The plexuses around the Malpighian corpuscles are particularly well developed. According to another view true lymphatic capillaries are replaced by terminal lymph spaces.

[2] Probably transitional epithelium really consists of only two layers as it appears to do when greatly extended. The upper layer would then be formed of multinucleate, epithelial cells with marked exoplasm. When contracted the deeper layer would appear to consist of several rows of cells. For details see p. 36 and Fig. 4.

The MUSCULATURE of the ureter is characterized by scattered bundles of smooth muscle fibers separated by considerable connective tissue. It is strongest in the lower part of the duct where it consists of inner longitudinal bundles, middle bundles of circular direction and outer longitudinal bundles. The latter usually are entirely lacking in the upper part of the ureter. On the other hand the part of the ureter which lies within the bladder wall, the so-called intra-mural portion of the ureter, shows only a single layer of muscle, a longitudinal layer of great thickness.[1] The muscle of the calyces and renal pelvis resembles that of the ureter. At the base of the renal papillae there is a slight thickening of the longitudinal musculature.

Pl. 63, Fig. 1 The mucous coat of the renal calyx is continued for a distance over the renal papilla; the latter is thus covered to its apex by a transitional epithelium which however is extremely thin. Over the apex of the papilla the transitional epithelium passes into a simple columnar epithelium which in turn is continued directly into the epithelium of the openings of the papillary ducts.

A tunica adventitia of loose connective tissue containing elastic fibers ensheaths the various parts of the urinary tract.

The structure of the **urinary bladder,** *vesica urinaria*, greatly resembles that of the ureter. The epithelium is the same in both organs and the mucous coat of the bladder shows the same features as does that of the ureter. Frequently it contains small rudimentary
Pl. 63, Fig. 4 lymph nodules. A true "submucosa" is not to be distinguished from the mucous membrane,
Pl. 64, Fig. 1 which in its deeper parts occasionally contains adipose tissue. A tunica muscularis mucosae is lacking although indications of one are said to be occasionally present. Glands do not occur except at the base of the bladder where they have been found in small numbers.

At the base of the bladder there are true glands which so greatly resemble those of the prostate that they may well be considered as displaced prostatic glands. In other parts of the bladder there are occasionally found in adults small epithelial depressions containing a colloid-like secretion, also indications of small crypts. As in the ureter true glands are completely absent.

The MUSCULATURE of the urinary bladder is much heavier and more compact than that of the ureter but shows the same subdivision into inner and outer longitudinal and middle circular layers. These layers, particularly the inner layer, show a distinct netlike arrangement of their fibers. There are no sharp boundaries between the layers which interlock in many places. The upper and posterior parts of the bladder wall show a serous coat derived from the peritoneum; elsewhere the bladder, like the ureter, has a tunica adventitia.

The **female urethra** in its lower portion usually has a stratified squamous epithelium, or occasionally a stratified columnar epithelium; but in its upper part the epithelium is of the ordinary transitional type. Towards its lower termination it contains scattered MUCOUS GLANDS. The mucous coat contains large numbers of veins which form plexuses. The musculature is extremely heavy and consists of inner longitudinal and outer circular bundles; in some places its inner layer is traversed by venous plexuses. The erectile tissue of the female urethra is formed by the venous plexuses and is termed a corpus spongiosum.

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[1] This longitudinal muscle is independent of the musculature of the bladder. By its contraction the termination of the ureter is opened and by its relaxation the opening is again closed. It thus acts as a valve-like mechanism for the orifice of the ureter. For details see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II.)

The **blood vessels** of the urinary tract form dense capillary networks close beneath the epithelium (see above); while the larger vessels for the supply of the mucous coat are to be found in the deeper layers of the submucosa. LYMPHATIC VESSELS are not found in the mucous coat proper but are present at the surface of the muscle where they form plexuses.

The **nerves** are in part sympathetic motor nerves which supply the musculature and in which scattered nerve cells may be observed; and in part are sensory nerves for the mucous coat within which they terminate intra-epithelially. Large numbers of interwoven and connected bundles of nerves are present, especially in the posterior wall of the bladder. Branches from these enter the muscular layers where they again divide and form plexuses. In the connective tissue between the urinary bladder and the seminal vesicle (p. 247) and in the adventitial connective tissue are numerous sympathetic ganglia in which small groups of from two to four nerve cells may regularly be observed. Similar ganglia are somewhat less frequently found in the muscular coat. A distinction may be made between the intramural and the extra-mural ganglion cells of the bladder wall. The latter are particularly well developed in the lower portion of the trigonum vesicae. Masses of cells also lie at the points where the ureters enter the bladder. Vater-Pacinian corpuscles are found in the adventitial connective tissue.

As to the male urethra, see under organs of reproduction.

VIII. The Male Reproductive Organs

1. The Accessory Glands of the Male Reproductive Organs

These comprise the prostatic gland, *prostata*, and the glands of Cowper, *glandulae bulbo-urethrales*.

The **prostate gland** is an organ composed of glandular tissue with a large quantity of smooth muscle and relatively little connective tissue. It surrounds the first part of the Pl 64, Figs. 2, 3 male urethra. The body of the prostate gland consists of a number (30—50) of branched tubulo-alveolar glands from which emerge 15—20 separate excretory ducts to empty into the urethra. These ducts have relatively wide, often indeed remarkably wide, lumina and are lined by a single layer[1] of cubical or columnar epithelial cells. The cells do not give the reactions of mucus but in many respects resemble serous cells. They frequently are slightly granular, and occasionally contain pigment. Such granules as are present are of a lipoid nature. The wide lumina of the prostatic gland, particularly in later life, contain concretions of spherical or ellipsoidal form and of brownish colour. These are the so-called *corpora amylacea* and are built up of concentric layers. Occasionally they reach a diameter of almost one millimeter but usually are rather smaller; only in exceptional cases do they become calcified.

The greater part of the prostatic gland lies posteriorly in the two lateral lobes of the organ. As a rule there are no glands anterior to the urethra and laterally from it only a few glands which are quite small. Between the glands are found bundles of smooth muscle fibers,[1] separated by connective tissue which contains numerous elastic fibers and comparatively few fibers of collagenous nature. A layer of elastic fibers lies immediately beneath the epithelium.

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[1] Occasionally the epithelium appears to contain more than one row of cells but in reality it never is stratified; although recently deep-lying, replacing cells have been described in addition to the columnar cells. The epithelium frequently forms small folds which project into the lumen after the fashion of villi.

Of the excretory ducts of the prostatic gland a few (2—3) are larger than the others and are lined by an epithelium (transitional epithelium) similar to that of the prostatic portion of the urethra. The remaining 15—20 ducts are smaller and are lined by columnar epithelium. In addition the larger parts of the two ejaculatory ducts (p. 246) lie in the substance of the prostate as does also the rudimentary male uterus which is represented by the *sinus prostaticus*, a simple tubule lined by ciliated epithelium and usually expanded at its blind end.

The BLOOD VESSELS and LYMPHATICS of the prostate are abundantly developed but show no peculiarities. Here as in the seminal vesicles the NERVES bear many ganglion cells.

The **glandulae bulbo-urethrales** (Cowper's glands) are of the tubulo-alveolar type, their terminal secreting parts being partly tubular and partly saclike. They contain cells which, like those of the smaller glands of the urethra, are essentially like the mucous cells of the salivary glands but have inter-cellular secretion canaliculi.[2] The excretory duct terminates in the cavernous portion of the urethra and shows irregular expansions; in general its structure resembles that of the urethral lacunae (p. 248). The branches of the ducts are lined by a simple cubical epithelium and pass into intermediate ducts which terminate in the secreting parts. The latter lie partly within the musculus transversus perinei profundus; consequently not only smooth muscle but also striated fibers are to be found the lobules of the gland.

2. The Testis, *testis*

The TESTIS, *testis*, is a compound, reticular, branched, tubular gland. It is surrounded
Pl. 65 by a dense connective-tissue coat, the tunica albuginea. On its posterior surface there is
Pl. 66, Figs. 1—5 found a wedge-shaped mass of connective tissue, the *mediastinum testis* (corpus Highmori), from which there run to the albuginea connective-tissue partitions, *septula testis*, some of which have a sagittal and others a horizontal direction. These septa contain numerous vessels and bound the individual pyramidal lobules of the testis. The lobules contain very loose connective tissue in which lies the true testicular parenchyma, the elaborately coiled tubules of the testis, *tubuli seminiferi contorti*. In man the interstitial connective tissue of the lobules contains in addition to vessels and nerves, a variable num-
Pl. 65, Figs. 1, 2 ber of large **interstitial cells** with comparatively small nuclei, but abundant protoplasm
Pl. 66, Fig. 4 which usually contains lipochrome pigment, and crystalloids.[3] The septa and the tunica
Pl. 4, Fig. 9 albuginea consist of dense connective tissue, rich in elastic fibers. Externally to the albuginea lies the visceral layer of the tunica vaginalis propria with its flat serous epithelium.

In many animals (*e. g.* the pig) the interstitial cells are very numerous and occupy almost as much space as the parenchyma itself; as a result the organ appears liver-colored on incision. The views as to the significance of these epithelioid cells are very diverse. In many quarters they are considered to be epithelial cells and the adherents of this view see in them an interstitial gland of internal secretion. However this view is contradicted by the results of embryology and of comparative anatomy as well as by experimental results. Consequently the interstitial cells must rather be considered as connective-tissue storage cells; the more so since the storage materials which they contain are identical with those of the supporting cells of Sertoli.[1]

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[1] The musculature of the prostate is intimately connected with the neighboring musculature of the bladder (sphincter vesicae internus). On the opposite side the organ is attached to the striated musculature of the floor of the pelvis (mus. sphincter urethrae membranaceae, see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II).

[2] The existence of these is questioned by many. This gland does not produce a purely mucous secretion but other substances are also formed by it.

[3] Smaller crystalloids are present in the cells of the tubules of the testis, the so-called crystals of LUBARSCH in the spermatogonia and crystals of SPANGARO in the SERTOLI cells.

The CONTORTED TUBULES OF THE TESTIS, *tubuli seminiferi contorti*, have a diameter of about 150—200 μ and usually begin with blind ends in the broader parts of the lobule near the albuginea. Occasionally the ends are forked and in some cases the tubules are connected in a netlike fashion. The tubules may reach a length of 50—75 cm. At the apex of the lobule, towards the margin of the mediastinum testis, several tubules join and pass into short and narrower canals (tubuli recti) which at first are slightly coiled but towards their terminations become quite straight. The tubuli recti represent the beginnings of the system of excretory ducts and are continued into the rete testis which lies in the mediastinum.

The WALL of the **seminiferous tubule** consists of several layers of epithelial cells the appearance of which varies with the condition of the organ as regards secretion (spermatogenesis). Surrounding the epithelium is a sheath[2] formed by several nucleated lamellae of connective tissue containing delicate elastic fibers. The epithelium has always a very considerable thickness while the lumen of the tubule varies from 40—60 μ in diameter. An extremely delicate basal membrane separates the epithelium from the connective-tissue sheath.

Pl. 65, Figs. 2, 4, 5
Pl. 66, Figs. 1—3

The EPITHELIUM of the seminiferous tubule contains two types of elements; 1. The so-called Sertoli cells, which are supporting (or nourishing) cells and do not participate, except indirectly, in forming the sperms. 2. Various generations of the cells whose final stage is the cellular secretion of the testis, *i. e.* the sperms or spermatozoa.[3] The supporting **cells of Sertoli** are stationary elements in the epithelium of the tubule, which in contrast to the generations of the germinal cells change little or not at all during the process of spermatogenesis. In particular they do not increase by mitotic division. They usually possess a clear pear-shaped nucleus with a large nucleolus, and very finely divided chromatin; while the cytosome is finely granular or finely striated and of irregular form. In mammals the nuclei almost always lie near the sheath of the tubule but in man they are separated from it by a considerable interval occupied by protoplasm. They are so placed between the spermatocytes or spermatogonia that the apex of the pear-shaped nucleus is turned towards the lumen of the tubule. The greater part of the cytosome of the Sertoli cell extends towards the lumen of the tubule in the form of a broad band which is finely striated (see below). At a certain stage of spermatogenesis the Sertoli cells together with a number of maturing sperms form a so-called spermatoblast (see below). In the functional organ they contain a variety of cell inclusions in addition to crystals (p. 238 footnote 3) and lipoid droplets. Some of the Sertoli cells are completely marked off from one another as separate elements, others have a syncytial connection.

Pl. 65, Figs. 4, 5
Pl. 66, Figs. 1—3.
Pl. 66, Fig. 3.

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[1] See Footnote 2, page 47.

[2] It should be noted that the collagenous fibrils in each of the 3—5 concentric lamellae have a similar direction in the same layer but that those of each two neighboring lamellae cross one another at right angles.

[3] The old name spermatozoon was given under a misapprehension as to the nature of these cells.

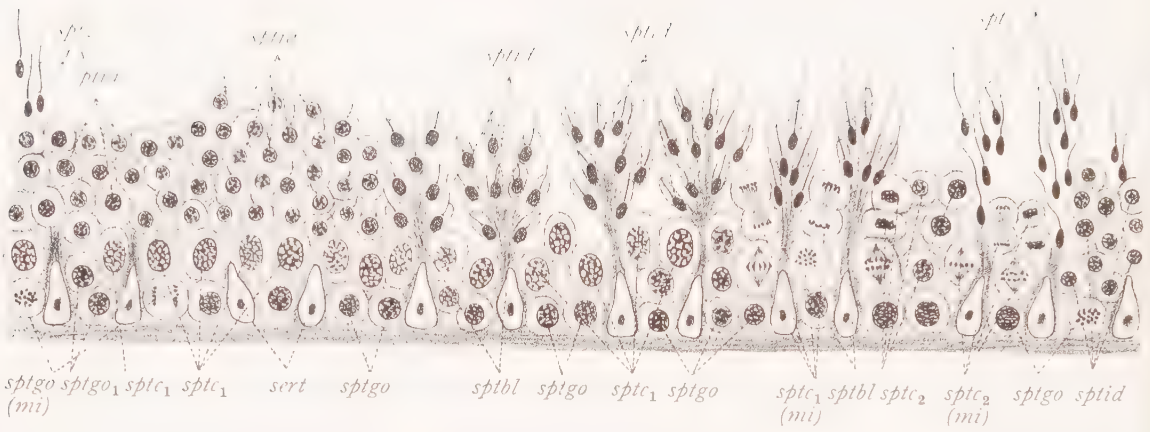

Fig. 34. **Diagram of the Process of Spermatogenesis.**

There is represented a spermatogenic wave which has entered from the left. Both right and left ends of the figure show the same stage. The process of sperm formation is shown in succesive stages from left to right.

(mi) = cells in mitosis
sert = supporting cells of Sertoli
sptbl = spermatoblasts
$sptc_1$ = spermatocytes I
$sptc_2$ = spermatocytes II
sptgo = spermatogonia
$sptgo_1$ = daughter cells of a spermatogonium becoming spermatocytes I

sptid = spermatids
(sptid) = spermatids in the first stage of transformation into sperms
[sptid] = spermatids in the second stage of transformation into sperms
sptz = sperms

The successive generations of cells involved in forming the male reproductive cells, the sperms or spermatozoa, which represent the true secretion of the testicular epithelium are first the primitive spermatic cells or SPERMATOGONIA. These increase by mitotic division and after growing quite large form the cells of the next generation, the SPERMATOCYTES OF THE FIRST ORDER (spermatocytes I). These in turn give rise by mitotic division to the SPERMATOCYTES OF THE SECOND ORDER[1] (spermatocytes II). Finally each spermatocyte of the second order divides mitotically into two SPERMATIDS which then become transformed directly into sperms (spermatozoa). Thus each spermatocyte I produces four spermatids and consequently four ripe male reproductive cells or sperms.

The positions of the spermatogenic elements in the testicular epithelium is such that Pl. 65, Figs. 4, 5 the spermatogonia rest upon the basal membrane of the tubule. Proceeding towards the Pl. 66, Figs. 1, 2 lumen there follow next the spermatocytes of the first order, then those of the second Fig. 34 order and finally, the spermatids arranged in several layers and bordering the lumen itself. The mitotic divisions of the spermatocytes, known generally as the spermatocyte divisions, are constantly found in large numbers in sections of secreting tubules. The first division, *i. e.* of the spermatocytes I, produces the spermatocytes II; the second division, *i. e.* of the spermatocytes II, produces the spermatids. As a rule the second division follows directly upon the first with only a very brief resting period between. The spermatocytes I are much larger than the spermatogonia; however the latter after dividing enter upon a relatively short period of growth[1] in which they gradually enlarge and become spermatocytes. The double division which rapidly follows produces relatively small cells, the spermatids.

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[1] This term indicates the parallelism in the maturation of sperms and ova (spermatocyte I = oöcyte I, spermatocyte II = oöcyte II).

The spermatocyte divisions correspond to the maturation divisions of the egg cell and on this account are also known as MATURATION DIVISIONS. Beside serving to increase the number of spermatids they also effect the reduction in the number of the chromosomes. Both sperm and egg at the time of fertilization contain the same number of chromosomes. By the union of the nuclei of the two germ cells towards the end of fertilization there is brought about a doubling of the number of chromosomes. The number of chromosomes of each species of animal can only remain constant from generation to generation if previously in each of the two germ cells, egg and sperm alike, there has been effected a reduction to one half of the number of chromosomes typical for the species in question. This reduction occurs through one of the two spermatocyte divisions; in many animals through the first, in others through the second division. Whichever it may be is then termed the reduction division[2] in contrast to the ordinary mitotic divisions — equation divisions — in which the number of chromosomes remains the same (p. 28).

The number of chromosomes appearing in the human spermatocyte divisions is said to be twenty-four. The spermatocyte nuclei are small at first and show the chromatin in a finely divided condition before the chromosomes form from the nuclear network. In the reduction division only twelve chromosomes (?) are said to appear as the reduced number. This would correspond to a normal count of only twenty-four chromosomes (pp. 22 and 28).

Pl. 65. Figs 4, 5
Pl. 66. Figs 1, 2
Fig. 34

The spermatogonia[3] are rather small and usually form a single layer. They have small cell bodies and large nuclei, rich in chromatin, by which they may easily be distinguished from the nuclei of the neighboring Sertoli cells which contain but little chromatin. The spermatocytes are large, spherical or polyhedral cells, with large cell bodies and large round nuclei which commonly display the prophases or more advanced stages of mitotic division. These spermatocytes form two to three layers, of which the outer contains the larger spermatocytes of the first order and the inner layer, nearer the lumen, contains the smaller spermatocytes of the second order. The spermatids, immediately after their formation through the second spermatocyte division, are small, spherical or polyhedral cells with little protoplasm but relatively large nuclei, rich in chromatin. However, they preserve this form for only a short time during which they begin to transform into the sperms (see below). In many animals, they possess a very distinct paranucleus (mitochondral body, p. 5) and a corresponding structure is also present in the human spermatid (see below).

The Semen, *Sperma*, and the formation of the Spermatozoa

The most important constituent of the seminal fluid,[4] particularly from the morpho-

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[1] This period of growth, in which falls the so-called synapsis *i. e.* a concentration of chromatin at one side of the nucleus, is definitely present in spermatogenesis and corresponds to the growth period of oögenesis; which however is much longer because the egg cell attains a much greater size than does the male germ cell. The spermatocyte divisions do not follow immediately upon the divisions of the spermatogonia; consequently one spermatogonium does not directly form eight spermatids, but rather a single spermatocyte I forms four spermatids.

[2] This reduction does not occur simply by failure of the chromosomes to divide in one of the spermatocyte divisions; but the chromosomes appear for this division in the reduced number (pseudo-reduction) through their conjugation in pairs during synapsis.

[3] Since after division the spermatogonia gradually grow to be spermatocytes it is often difficult to distinguish between the two varieties of cells.

[4] The seminal fluid as discharged by ejaculation consists not merely of sperms but also of the secretion of the accessory reproductive glands, the prostate, the seminal vesicles and the bulbo-urethral glands (p.244). In addition the testis supplies an internal secretion (see below) which is probably formed by the seminiferous tubules themselves.

Pl. 66, Fig. 5 logical point of view, is the secretion of the testis. The **sperms** (SPERMATOZOA) are cells each of which has a long, threadlike flagellum. Three chief parts are to be distinguished Fig. 35 in the sperms of most animals, including man: 1. the HEAD (or better, the body); 2. the middle- or CONNECTING-PIECE, the anterior part of which is known as the neck; 3. the TAIL. In man the entire sperm measures from 50—65 μ in length, of which the head occupies 4—5 μ, the middle piece about the same while the remainder forms the long tail.

The head has the form of an elliptical disc which is thinner anteriorly than posteriorly and is about 5 μ in length and 2—3 μ in breadth. In profile the head of the sperm looks pear-shaped, the anterior, pointed end measuring 1.8 μ in thickness while the posterior end is more than 3 μ thick. The sperms of most animals have, at the anterior end, an especially hard cap-like structure which serves as a perforatorium. Since the head of the sperm is derived almost entirely from the nucleus of the spermatid, it stains intensely with nuclear dyes. In addition to the pure chromatin in the head of the sperm there is also a fine sheath of protoplasm. The sperm, by its mode of formation, thus corresponds to a cell with eccentric nucleus. The middle-piece of the sperm is rather longer than the head, but decidedly more slender (1 μ in width). It is almost exactly cylindrical and consists of an anterior part, the neck, and a posterior part, the connecting-piece in the narrower sense; however in the human sperm both parts are intimately joined. The neck is formed of a short protoplasmic piece containing the centrosome which consists of anterior and posterior elements (diplosome). The connecting-piece proper contains in its interior the first portion of the axial thread which, in this part of its course, is still surrounded by a relatively thick protoplasmic sheath. In the latter there lies a spiral thread which has been looked upon as the chondriome of the cell (p. 4).

Pl. 66, Fig. 5 The tail is the longest, but thinnest part of the sperm, diminishing gradually in thick- Fig. 35 ness towards its free end. Near the connecting-piece it measures about 0.75 μ and at its extreme end about 0.25—0.1 μ. Of the entire length of the tail (50 μ), about 40 μ is occupied by the CHIEF-PIECE and about 10 μ by the END-PIECE. The latter represents the bare axial thread and begins at the posterior part of the neck continuing through the connecting-piece and also through the chief-piece of the tail, within which it is still surrounded by a special sheath.[1] Only the axial thread is capable of movement. The ability to move persists after discharge from the human body and is increased by weak alkaline solutions and suspended by acid solutions.[2] The movements take the form of strong lashing and bending motions of the tail while at the same time the whole sperm revolves on its longitudinal axis. The stimulus for movement proceeds from the middle-piece, consequently even sperms whose heads have been broken off will continue to move. Since the middle-piece contains the centrosomal apparatus and the axial thread proceeds from one of the centrosomes there is here a pronounced parallelism with ciliated cells, the basal corpuscles (p. 13) of which have also been considered as centrosomes. Beside the normal sperms, abnormal forms are frequently observed, some with two heads and others with two tails.

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[1] In many animals the structure of the sperm is decidedly more complicated than it appears to be in man. Thus, even in many mammals, the axial thread is surrounded by a spiral membrane much more highly developed than in man (see below).

[2] It is uncertain how long the human spermatozoa may live in the female genital tract after ejaculation. This is a matter of considerable variation in animals.

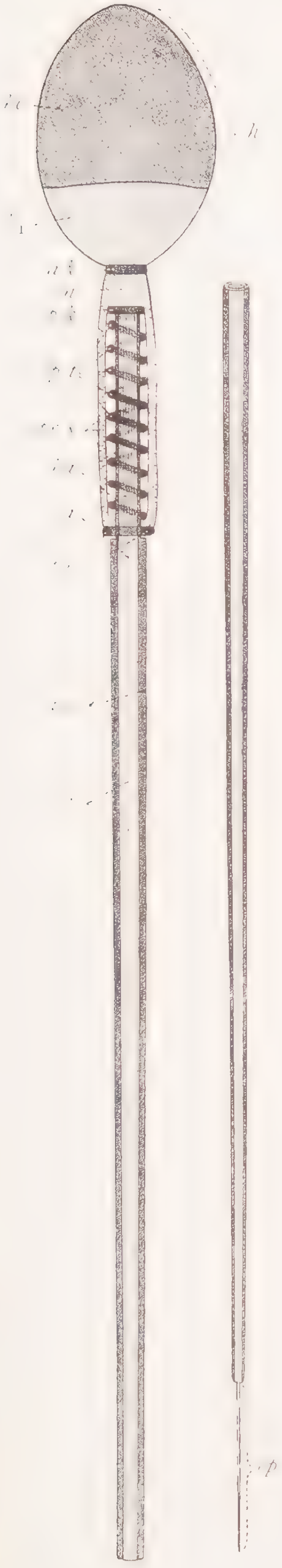

Fig. 35. **Diagram of the Structure of a Human Spermatozoon** (after MEVES).

The posterior half of the tail is represented on the right. The figure displays many features of the structure of the sperm which can only be recognized with the aid of special methods and very powerful magnification, for instance the finer structure of the connecting-piece.

a = axial thread
a k = anterior knob of neck
a s = sheath of axial thread
ep = end-piece
h = head
h_1 = posterior part of head
hc = head-cap
n = portion of neck between knobs
p k = posterior knob of neck
pr s = protoplasmic sheath of connecting-piece
sp t = mitochondral, spiral thread
t r = terminal ring of connecting-piece

The **formation of the sperms** from the spermatids proceeds essentially[1] by a progressive concentration of the chromatin network of the spherical spermatid nucleus and by its simultaneous elongation to form the head of the sperm. In this process the nucleus moves to that end of the cell which is turned away from the lumen and there elongates until it assumes its definite form. The axial thread develops quite early in the differentiation of the spermatid, as a slender thread which grows from the distal one of the two diplosomes which together form the centrosome of the spermatid. The other, the proximal diplosome, lies at the base of the head where head and neck join. The sheaths which surround the axial thread in the connecting-piece and in the chief-piece of the tail are derived from the remaining protoplasm of the spermatid. A narrow border of protoplasm also surrounds the nuclear substance of the head. In addition to the centrosomes the connecting-piece (see Fig. 35) contains also the mitochondral apparatus of the sperm in the form of a spiral thread.

During this transformation of the spermatid into the sperm Pl. 66, Fig. 3
there occurs the temporary union of a number (about 15—20) of maturing sperms with the protoplasm of a Sertoli cell. In this process the maturing sperms move more towards the periphery of the tubule and sink into the protoplasmic processes of the supporting cell, producing a picture somewhat like the fingers of a glove. This has been termed a COPULATION and is considered to be the method by which the maturing sperms are nourished. The entire picture formed by the copulation, *i. e.* the Sertoli cell together with the maturing sperms connected with it, is named a SPERMATOBLAST. During maturation the sperms enter so deeply into the protoplasm of the spermatoblast as to lie near its nucleus. Later they withdraw and at the end of maturation lie close to the lumen.

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[1] It is not possible here to go into the finer details and relationships, some of which are at present matters of dispute.

The process of spermatogenesis takes the form of a SPERMATOGENIC WAVE, that is Fig. 34 to say in a transverse section of a seminiferous tubule approximately the same stage of spermatogenesis appears in all parts of the wall. On the other hand in longitudinal sections the individual phases, up to the completely matured sperms, are observed in succession; as a result all stages of the formation of sperms may be seen simultaneously in the same seminiferous tubule. Since the process is many times repeated within the same seminiferous tubule, spermatogenesis proceeds in a wave-like manner.

The spermatic fluid as discharged consists not only of the secretion of the testis, that is of sperms, but also of the fluid secretions of the accessory glands (epididymis, seminal vesicle, prostate etc.). Morphologically their secretions being fluid are not as a rule to be distinguished, but prostatic concretions (p. 237), if passed in the seminal fluid, are easily recognized by their concentric structure. Although a matter of individual variation as a rule the number of sperms is very great. In man, several million sperms are usually present in one cubic millimeter of the spermatic fluid; although the number diminishes progressively in closely successive ejaculations.

The sperms are formed only in the contorted tubules, while the so-called **straight** (that is to say, no longer convoluted) **tubules** lying in the mediastinum testis act as ex- Pl. 65, Fig. 3 cretory ducts for the secretion of the testis. Frequently, but not invariably, the tubuli contorti of large diameter and wide lumina are continued by means of a short, straight, connecting piece of small diameter, the *tubulus rectus*, into the so-called rete testis, but the transition is often direct.[1] The tubuli recti (20—60 μ in diameter) have at first a columnar, then a cubical, epithelium which develops from the Sertoli cells of the tubuli contorti; while the tubules of the *rete testis* with about the same diameter have low cubical or flat cells; like the Sertoli cells, they contain fat droplets. Thus their diameter, though varied, is much less than that of the tubuli contorti and their walls are much thinner than those of the latter. The tubules are embedded in dense connective tissue containing numerous blood vessels.

The larger **blood vessels** of the testis lie in the septa and the mediastinum, while smaller branches enter the lobules and break up into capillary networks which surround the tubuli contorti. The LYMPHATIC CAPILLARIES behave similarly and pass into a plexus of lymphatic vessels which lies beneath the tunica albuginea. The **nerves** are of sympathetic origin; they run with the blood vessels and thus reach the seminiferous tubules. Probably they penetrate the membrane of the latter to end freely between the epithelial cells.

3. The Seminal Ducts

The seminal ducts comprise the rete testis which lies within the testis proper, the epididymis, the ductus deferens, the seminal vesicle and the ductus ejaculatorius.

Pl. 65, Fig. 1 The tubules of the head of the **epididymis,** *ductuli efferentes testis*, differ markedly in Pl. 66, Figs. 6—8 structure from the *ductus epididymidis* which forms the remaining parts of the epididymis (for details see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II). The efferent ductules are relatively wide tubes (180—220 μ in diameter) with large lumina and a lining epithelium which is partly columnar and partly cubical. They are eight to fifteen in number and proceed directly from the tubules of the rete testis, the diameter of which is much less. The columnar cells bear cilia which however are not present on the cubical cells. The latter are distributed in groups among the former in such fashion as to form small depressions or furrows which affect only the epithelium and do not as a rule produce corresponding ridges on the membrana propria. The cubical cells which lie at the bottom Pl. 66, Fig. 7 of the depressions are regarded as rudimetary alveolar glands. However the depressions, which usually are furrows between longitudinal folds, differ very greatly in individuals in the degree of their development or according to their functional condition. Occasionally they are entirely lacking. The epithelial cells of the epididymis often contain yellowish pigment (lipofuscin) which occurs most frequently in the columnar ciliated cells; other granulations are also present. Beneath the epithelium lies a membrana propria and usually a stratum of smooth muscle fibers which consists of only a very few layers and is permeated by fine elastic fibers.

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[1] The transition of the tubuli contorti into the straight, efferent tubules is variable and may be highly complicated. In some cases intermediate parts occur and in other cases are lacking. Moreover it is not always the extreme end of the tubulus contortus which unites with the tubulus rectus but the latter may connect with the side of the former.

The numerous convolutions[1] of the *ductus epididymidis* form the body and tail of Pl. 66, Fig. 8 the epididymis, the total length of the duct being about 2.5 m. The duct is lined by a char- Pl. 3, Fig. 4 acteristic epithelium of great thickness although the epithelial cells themselves are arranged in only two rows. The diameter of the duct is greater than that of the efferent ducts (250 to 400 μ) but because of the thickness of the epithelium the lumen is relatively narrow. The cells next to the lumen are very long, slender and columnar. The elongated, sausage-shaped nuclei alternate, or rather are placed at different levels. The cells bear long (about 30 μ), flagellum-like, immobile processes (stereocilia)[2] which project far into the lumen of the duct. The thickness of the epithelium depends upon the stage of secretion and varies from 30—80 μ. Each cell because it is so narrow, bears only a relatively small number of cilia. Basal corpuscles are not present, but terminal bars show distinctly. The cells possess secretory powers, the antecedents of the secretion being contained in the protoplasm in the form of granules; while the cilia conduct the secretion into the lumen. Within the lumen of the duct there are to be found great quantities of ripe sperms in addition to the secretion formed locally. Owing to the relatively wide lumen and the great length of the duct (2.5 m.) its numerous convolutions are able to shelter an enormous number of sperms, estimated at several thousands of millions. The duct consequently serves, by virtue of its exceedingly numerous convolutions, as a receptaculum seminis. In addition it supplies a secretion of its own.[3] Beneath the long slender "hair cells" is a low, interrupted layer of round or somewhat flattened cells which rest immediately upon the membrana propria. Then follows a dense layer of lamellar connective tissue and a few circular layers of smooth muscle fibers. The quantity of this muscle increases towards the tail of the epididymis within which a discontinuous layer of longitudinal muscle bundles may be distinguished.

The **ductus deferens** is a long tube with an extremely muscular wall and relatively Pl. 67 narrow lumen. Its diameter may be as much as 2½—3½ mm., but the diameter of its Pl. 68, Fig. 1 lumen measures only 0.4—0.5 mm. Its epithelium consists of two rows of cells, a superficial row of short, columnar, ciliated cells[1] beneath which is a row of flat or rounded cells. A true tunica submucosa is lacking. The mucous coat contains no glands. In the outer layers of the duct there are numerous elastic fibers which form a few weak, longitudinal folds. The muscular coat is very strongly developed and forms almost nine tenths of the entire thickness of the wall. Its layers vary in different regions of the duct. At its beginning near the epididymis it consists of an inner longitudinal layer, a middle circular layer and an outer longitudinal layer. Commonly in its terminal portion there is still present a thin, inner circular layer but the demarcation of the remaining layers is usually somewhat indistinct.[2] External to the muscular coat is a tunica adventitia of loose connective tissue containing elastic fibers, while within the spermatic cord longitudinal bundles of smooth muscle are commonly present as well and form the internal cremaster muscle.

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[1] Within the tail of the epididymis the convolutions are less numerous. Because of the convolutions the duct is cut through many times even in a single section of the epididymis.

[2] Due to the process of preservation the cilia usually become stuck together in bunches.

[3] Certain relatively large, multinucleate cells have been found in the epididymis and because they apparently phagocytose sperms have received the name of spermatophages. However this is not really a question of phagocytosis but of an agglutination of sperms in which other cells may also be involved.

The ductus deferens forms the chief constituent of the spermatic cord, *funiculus* Pl. 67, Fig. 1 *spermaticus*, which beside the different sheaths contains numerous veins, (plexus pampiniformis) which are provided with valves and bear an unusual quantity of muscle in their walls (for details see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II).

The **ampulla of the ductus deferens** and the **vesicula seminalis** are alike in structure, Pl. 68, Figs. 2—4 inasmuch as the mucous coat forms very complicated folds upon which there rest secondary folds. Long diverticula of the mucous coat are frequently present and often assume the character of branched glands sinking deep into the muscular coat. All these appearances are much more marked in the seminal vesicle than in the ampulla. The thickness of the epithelium varies. On the larger folds it often consists of two layers, but in most situations it is a simple columnar epithelium without cilia becoming simple cubical epithelium in the depressions. All the cells contain yellowish brown pigment granules. The structure of the tunica propria corresponds to that of the ductus deferens but its content of elastic fibers is still greater. The layers of the muscular coat are very irregular both in the ampulla and in the seminal vesicle, transverse and longitudinal strands alternating with oblique fibers. The thickness of the muscular coat is relatively much less in the seminal vesicle than in the ductus deferens. Externally the seminal vesicle is surrounded by a loose adventitial connective tissue which bears numerous vessels, nerves and sympathetic ganglia (see below).

The **ductus ejaculatorius** shows structural features similar to those of the seminal vesicle, its mucous coat, like that of the latter, possessing evaginations or diverticula, Pl. 64, Fig. 4 but in smaller number. The epithelium is the same as that of the seminal vesicle but a muscular coat proper is lacking, the wall consisting only of connective tissue embedded within the muscle of the prostate.

The secretion of the seminal vesicle is a viscous fluid. The seminal vesicle ordinarily contains no spermatozoa and consequently does not represent a retinaculum seminis. It is highly probable that the small number of sperms which may be found sometime after death in the lumen of the seminal vesicle have migrated there post mortem, since an examination of the seminal vesicle immediately after an execution does not reveal their presence. In many animals (rodents, such as the mouse and the guinea pig) the secretion of the seminal vesicle is discharged after the semen proper. It then coagulates into a firm mass, the vaginal plug, which closes the vagina for about twenty four-hours. The seminal vesicles of these animals are very greatly developed.

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[1] The epithelium of the ductus deferens, like that of the urethra, is subject to numerous individual variations. The cilia are frequently lacking and in their place there appears a cuticular border, or the columnar epithelial cells may be present in but a single row instead of the usual two rows, even transition epithelium (?) may be found.

[2] In particular the muscle fibers are separated by relatively large quantities of connective tissue. The muscular wall of the ductus deferens is thus firm in contrast to that of the ureter.

The BLOOD AND LYMPHATIC VESSELS of the spermatic ducts show no peculiarities. The NERVES in the region of the seminal vesicle and ductus deferens are distinguished by numerous small sympathetic ganglia lying between the muscular layers of the organ. Motor fibers from this plexus myospermaticus run to the musculature of the organs and sensory fibers to the mucous membranes. In the tissues surrounding the organs, particularly in their adventitial coats, there are also found stout sympathetic nerve trunks with ganglia of greatly varying size. In the muscular layer of the seminal vesicle there is present a very delicate nerve plexus of singular regularity of form.

The small, rudimentary appendages of the male reproductive organs have the following structure: the *paradidymis* (organ of Giralde's) and the *ductuli aberrantes testis* have a ciliated epithelium and a thin wall of connective tissue. The *appendix testis* (hydatid of Morgagni) is a solid body covered with ciliated epithelium and formed of connective tissue which contains numerous blood vessels; while its stalk is hollow and is lined by columnar epithelium. The so-called stalked hydatid, *appendix epididymidis*, on the other hand is a hollow vesicle lined by a cubical epithelium (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II).

4. Penis and Male Urethra

The erectile bodies of the **penis,** *the corpora cavernosa penis*, are covered externally by a very thick and firm tunica albuginea which has a thickness of 1.5—2 mm. and consists of dense connective tissue, very poor in cells but rich in fine elastic fibers. Between the erectile bodies of the two sides lies the *septum (corporum cavernosorum) penis* formed by the tunicae albugineae. The cavernous tissue consists of trabeculae which anastomose abundantly and which are formed of connective tissue and bundles of smooth muscle. The cavities so formed communicate with one another, are lined with endothelium and contain blood. They stand in direct connection with the veins on the one hand and with the arteries or the capillaries on the other. Pl. 69

The arteries of the penis are distinguished by their unusually thick walls. In part they give rise to capillaries which form a plexus (superficial plexus) which lies beneath the albuginea. In part they form a deeper, coarser plexus (deep plexus) from which the arterial blood goes directly into the cavernous spaces without passing through capillaries. The smaller arteries, the so-called helicine arteries, are especially distinguished by thickenings of the tunica intima which are able to block the arteries completely. The efferent veins, *venae emissariae*, collect the blood partly from the deep plexus, partly from the central cavernous sinuses and return it chiefly by the unpaired vena dorsalis penis (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II).

The skin of the penis, while almost devoid of fat, is merely a part of the external skin and shows exactly the same structure as the latter; although as a rule there is a more or less marked amount of pigment in the epidermis. In the preputium, which resembles a mucous membrane, hairs are completely absent although there are found independent sebaceous glands, the so-called Tyson's glands, glandulae praeputiales. Scattered strands of smooth muscle are present in the deeper parts of the preputial skin. Pl. 88, Fig. 5

The structure of the *corpus cavernosum urethrae* differs in many regards from that of the corpus cavernosum penis. In the first place, the greater part of the body is traversed by the urethra which occupies an almost exactly central position. In the second place, it is surrounded by a much weaker tunica albuginea which is formed of circular strands only. Thirdly, the entire thickness of the body is not formed of true cavernous tissue alone but the mucous coat of the urethra is succeeded by a kind of submucous tissue with numerous venous plexuses. Only in this situation is there a true cavernous tissue like the erectile Pl. 69, Fig. 4

bodies of the penis. In the posterior part of the corpus and in the bulbus there are arteries which pass directly into venous spaces.

The walls of the cavernous spaces are formed of connective-tissue trabeculae which contain elastic fibers and a considerable amount of smooth muscle. Toward the albuginea the size of the cavernous spaces diminishes and the musculature fails completely. In place of the cavernous spaces there appear wide veins and finally a capillary plexus. Otherwise the cavernous tissue corresponds to that of the erectile bodies of the penis. The anterior end of the corpus cavernosum urethrae forms the glans penis and does not consist of cavernous tissue but of plexuses of looped and intertwined veins held together by strongly developed fibro-elastic connective tissue, the strands of which are partly circular, partly radial in direction. The skin which covers the glans is firmly attached to the substratum and contains very long papillae, which in the region of the corona glandis project with their epidermal covering, thus producing the peculiar roughness of the surface of this part of the glans.

The **male urethra,** *urethra virilis*, according to its development consists of two different parts. The urethra proper forms only the first portion or the prostatic part; the remaining portion is the much elongated sinus urogenitalis. The EPITHELIUM of the urethra varies in its different parts, the first part — as far as the opening of the ductus ejaculatorii — like the upper parts of the urinary tract is lined by transitional epithelium. The remaining (and longer) portion usually has a stratified columnar epithelium, commonly of several rows of cells. However a simple columnar epithelium may be present and islands of stratified squamous epithelium are also found. These features of the epithelium show great variation in different individuals. The terminal portion, the fossa navicularis, bears a stratified squamous epithelium like that of the skin of the glans penis; papillae are also present in the mucous membrane. Pl. 69

The MUCOUS MEMBRANE OF THE MALE URETHRA (both pars membranacea and pars cavernosa) is rich in elastic fibers and passes into a poorly defined submucous layer. It contains many wide veins which are devoid of muscle and which form plexuses (see above). Glands are also present but not in great abundance. These urethral glands (of Littré) are of two types, small superficial glands and larger glands located in the deeper parts of the mucous coat. The latter type is found chiefly in the pars membranacea, the former predominate in the pars cavernosa. In this part of the urethra the glands — particularly the smaller glands — open into evaginations of the mucous membrane, the so-called lacunae urethrales (of Morgagni). All are mucous glands of irregularly alveolar form and frequently are so small that, like half-alveoli, they set in the sides and at the bottom of ductlike prolongations of Morgagni's lacunae. In the pars membranacea the alveoli of the deeper glands lie in the muscular layer where they may attain a very considerable size. The corresponding glands of the pars cavernosa lie with their alveoli deep within the cavernous tissue. Pl. 69, Figs. 1, 4

The FEMALE URETHRA corresponds in structure to the pars membranacea of the male urethra. However the glands, with the exception of a few gland-like lacunae, are lacking. On the other hand the musculature is strongly developed and the same is true of the veins of the mucous membrane (p. 236).

Only in the pars prostatica and pars membranacea is there a layer of smooth muscle incorporated in the wall of the male urethra. This layer is subdivided into inner longitudinal and outer circular parts and in the pars cavernosa gradually comes to an end, while single fibers and small bundles of fibers continue to be found in the tunica propria. In Pl. 69, Fig. 1

addition to the muscular coat the pars membranacea is surrounded by the striated muscle of the musc. sphincter urethrae membranaceae (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II).

The BLOOD VESSELS of the pars cavernosa of the urethra resemble those of the penis and the LYMPHATIC VESSELS have a corresponding course. The NERVES form both special and ordinary intra-epithelial terminations.

The glans penis contains numerous lymphatic vessels (those of the deeper layer being connected with the lymphatic vessels of the urethra) and its nerves are even more abundant. Beside free intra-epithelial endings there are present special terminations, the most important of which are the so-called genital corpuscles; but end bulbs and the tactile corpuscles of Meissner are also to be found.

IX. The Female Reproductive Organs

1. The Ovary, *Ovarium*

Even macroscopically the ovary is seen to be composed of a cortex and a medulla. Pls. 70—72

The CORTEX of the ovary is surrounded by a connective-tissue *tunica albuginea* consisting of crossed and interlaced bundles of stout fibers and is the site of the ovarian parenchyma. It contains also an abundance of dense connective tissue, the stroma ovarii, which passes gradually into the tunica albuginea. This connective tissue consists of collagenous fibers and quite numerous fibrocytes, but no elastic fibers are present. The MEDULLA is, so to speak, a prolongation of the hilum ovarii and is formed essentially from the vessels, and in particular from the many veins, which enter the organ in company with loose connective tissue containing both elastic fibers and scattered fibers of smooth muscle. Thus the glandular substance proper lies in the cortex, the medulla of the ovary merely providing nourishment for the functioning of the organ.

The SURFACE of the ovary is covered by the peritoneum, the connective tissue of which fuses with the tunica albuginea of the ovary. The peritoneal epithelium of the sur- Pl. 70, Fig. 1
face of the ovary is formed of low-columnar or cubical cells. The epithelium assumes this form most clearly in the ovary of the new-born and bears the name of GERMINAL EPITHELIUM because it is the source of the whole ovarian parenchyma. In adults the cells of the germinal epithelium are often flattened and consequently not so distinct as during youth. The fact that the peritoneal epithelium changes its character as it passes from the mesovarium to the ovary (retaining so to speak the embryonic character of the general peritoneal epithelium) causes a peculiar appearance as though the surface of the ovary were covered with mucous membrane. The view that the ovary has no peritoneal covering and represents a break in the continuity of the peritoneum is altogether erroneous.

The **cortex** of the ovary, as already mentioned, is traversed by numerous connective-
tissue bundles which join with the tunica albuginea. Between them lie the ovarian follicles, Pl. 70, Figs. 1—3
folliculi oophori, *(vesiculosi* — Graaf) in different stages of development, the youngest stages lying next to the albuginea. At any one time there are to be found only a very small number of follicles in the stage of complete or almost complete development. The great majority of the remaining follicles attain their final development gradually and after the lapse of considerable time.

The process of the formation of ova and follicles may be observed in the new-born and for some time after birth, but is largely completed during embryonic life; later, especi-

ally in adults, no further formation of ova and follicles takes place. Certain cells of the germinal epithelium on the surface of the ovary increase in size, particularly by growth of the cytosome, and become quite large, spherical cells, the so-called primordial (primitive) ova. Usually several primordial ova now form a rod-like mass which grows into the stroma of the cortex and which contains clumps or *nests of ova* surrounded by germinal epithelium (so-called egg-tubes[1] of Pfluger). Within the nests of ova each primordial ovum is surrounded by a single layer of flat or flat-cubical cells of the germinal epithelium
Pl. 70, Fig. 1 (later the FOLLICULAR EPITHELIUM) and thus constitutes a PRIMORDIAL OR PRIMITIVE
Pl. 71, Fig. 2 FOLLICLE *(folliculus oophorus primarius)* the diameter of which measures about 30—40 μ.

The greater number of the primitive follicles lie close beneath the tunica albuginea
Pl. 70, Fig. 3 in the most external layer of the cortex and there form a narrow band parallel to the surface of the ovary.

The growth of the ovarian follicle now follows, primarily by MULTIPLICATION OF ITS EPITHELIAL CELLS; as a result the ovum becomes surrounded by several layers of
Pl. 70, Fig. 3 cells which form the so-called membrana granulosa. At the same time a connective-tissue capsule, the *theca folliculi*, is formed around the whole follicle by the ovarian stroma.
Pl. 71, Figs. 2—4 The ovum is now surrounded by a membrane which may appear structureless or marked by fine radial striations. This membrane is termed the OÖLEMMA, zona pellucida or better membrana pellucida. It arises as a product (cuticle, see p. 14) of the cuticular epithelium surrounding the ovum and increases considerably in thickness during the growth of the Graafian follicle.

Accompanying the further growth of the ovarian follicle and a further increase of the follicular epithelium by mitotic division, there takes place on the part of the follicular epithelium the secretion of a fluid, the liquor folliculi. This is a process of true secretion by the epithelial cells and is not accompanied by their destruction. The secretion appears at one or more points which lie more or less distant from the centre of the follicular epithelium. Consequently the ovarian follicle now assumes the form of a vesicle **(folliculus vesiculosus)**, while at the same time there occurs a great increase in the size of the follicle as a whole. In this process the ovum is usually pressed against the wall by the eccentric and continued accumulation of fluid. Thus the ovum often lies surrounded by follicular
Pl. 70, Figs. 2, 3 cells but connected with the epithelium of the wall only by epithelial cords. The follicular
Pl. 71, Figs. 3, 4 epithelium in general consists of several layers of rounded or polygonal cells; although the outer cells bordering on the theca folliculi and those which lie next to the ovum, in contact with the oölemma, are columnar. The cells in the latter position form the so-called corona radiata while the mass of epithelium, which as a whole surrounds the egg, is termed the *discus (cumulus) oophorus* (ovigerus). When the follicle bursts, this mass of epithelium is discharged along with the ovum. The theca folliculi of the larger follicles is subdivided into an external fibrous layer containing numerous cells and but few fibers, the theca
Pl. 70, Fig. 3 interna, to the inner side of which is a connective-tissue, hyaline membrane (see below). The theca interna consists of connective tissue which contains few fibers, but many blood vessels and cellular elements rich in protoplasm. True fat droplets are commonly present in these cells as well as lutein granules (see below).

The mature Graafian follicle which is ready to burst may have a diameter of 1 cm. or even more and consists of: 1. the theca folliculi interna and externa, *i. e.* the connective-tissue capsule containing blood vessels for the nourishment of the follicle; 2. the follicular epithelium, also known as the membrana granulosa. This being a true epithelium is devoid of blood vessels and in follicles of medium size consists of several layers of cells, but in mature follicles becomes reduced to one layer at the point where distension will cause the break to occur. A delicate, structureless, basal membrane, the so-called hyaline membrane, separates the epithelium from the theca folliculi; 3. the ovum. The latter is a truly spherical cell which increased considerably in size during the growth of the follicle and now contains an abundance of protoplasm. When the follicle is mature the ovum has attained a diameter of about 150 μ, according to some measurements even more. It lies within the spherical cavity of the oölemma (membrana pellucida) which it completely fills. That the human ovum possesses a cell membrane of its own is improbable. In mammals the large protoplasmic body of the ovum contains inclusions, the quantity of which varies greatly in different species. These inclusions appear partly in the form of coarse granules or droplets which consist of lipoid substances (yolk) and partly of delicate mitochondria of deutoplasmic or lipoid nature.[1] In contrast to the protoplasm proper these inclusions are given the name of DEUTOPLASM and in the large-yolked eggs of birds, reptiles, amphibia and many fishes they occupy the greater part of the entire ovum. The deutoplasmic structures of the human ovum lie chiefly in its central parts. The nuclei of the ova of the larger follicles are almost exactly spherical and usually lie in an eccentric position. Their diameter is about 30—40 μ and as a rule each contains a very fine chromatin network and a nucleolus 7—10 μ. The latter was formerly known as the germinal spot *(macula germinativa)* and the nucleus as the germinal vesicle *(vesicula germinativa)*.

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[1] Usually these outgrowths are solid, not hollow.

Pl. 71, Fig. 1

The ovum of the growing Graafian follicle must be considered an oöcyte of the first order (cf. spermatogenesis p. 240) in its growth period which lasts until shortly before the rupture of the follicle. It then enters upon the first maturation division, the results of which are an oöcyte of the second order and the first polar body. In this condition — as oöcyte II — the ovum is capable of fertilization and by rupture of the follicle is discharged into the oviduct[2] (for details see textbooks of embryology). The oögonia, corresponding to the spermatogonia, are no longer to be found in the adult ovary which contains only oöcytes in different stages of the growth period. Thus the stage of synapsis in the nucleus of the oögonium (p. 241 footnote 1) falls within the earlier periods of the development of the ovary.

Rarely in man, but frequently in mammals, follicles are found which contain two ova. Ova with two nuclei (germinal vesicles) have also been observed. Such ova only occasionally succeed in maturing and then form two maturation spindles. In the formation of the liquor folliculi vacuoles often appear around which the neighboring cells become arranged radially. These structures are known as CALL-EXNER bodies and have been confused with supernumerary ova.

Pl. 71, Fig. 4

The larger the maturing follicle becomes, the more deeply does it sink into the interior of the ovary; but as the secretion of fluid continues and the follicle becomes more and more distended, the superficial part of its wall again approaches the surface of the ovary. Just before rupturing the follicle attains a diameter of 8—12 mm. and occupies the full breadth of the cortex. The outer part of the follicular wall becomes greatly thinned and finally ruptures leaving in the surface of the ovary a tear which later heals.[3]

Pl. 70, Fig. 2

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[1] In addition to the nucleus the maturing ova of mammals, including man, contain another small structure, the so-called yolk nucleus. It probably represents a relic of the centrosome which ordinarily has disappeared from the ovum when maturation is complete.

[2] This is the case with most mammals and probably also in man. However in the dog discharge occurs while the nucleus is in the resting condition and while the ova are as yet oöcytes of the first order.

[3] In many mammals the closure of the tear occurs almost instantaneously, as a result the formation of liquor continues; but in man and in many other mammalls the break remains open and visible for a considerable time.

The human ovary, like that of many animals, contains, in addition to an almost purely connective-tissue stroma, certain large, interstitial cells, the origin of which is as yet uncertain. According to the views of many authors, they are collections of connective-tissue cells, rich in protoplasm and are akin to those of the theca interna of the Graafian follicle. According to others this cell-complex represents a kind of gland with an internal secretion (INTERSTITIAL OVARIAN GLAND). Proof of the latter view has not been given and is particularly needed since the cells are of connective-tissue origin and the view is thus a priori improbable (p. 239). The number and size of this cell-complex undergoes many changes according to the age of the animal and the functional condition of the organ. As mentioned the interstitial cells of the human ovary, in contrast to those of many animals, *e. g.* the rabbit, are present in remarkably small numbers. Indeed at the time when follicles are maturing they are scarcely to be found. On the other hand during childhood they are present somewhat more abundantly. Also during pregnancy, while the maturation of the follicles ceases and those which are partly matured suffer atresia, the number of these cells is decidedly increased; presumably because the cells derived from the theca interna of the atretic follicles are identical with the cells in question.

Pl. 71, Fig 5

Pl. 72

The **rupture of the follicle** is followed by the collapse of its walls. The parietal follicular epithelium which remains now becomes hypertrophied and the cells attain many times their original size. In many mammals and in the human ovary the number of cells also increases, in some cases to a very considerable extent. At the same time connective-tissue buds containing blood vessels from the theca folliculi[1] press inward between the epithelial cells. The resulting structure is called the **corpus luteum** because of its intensely yellow color which depends upon the early appearance within the hypertrophied cells not only of true fat droplets but also of droplets of a yellowish, lipoid pigment named lutein.[2] The hypertrophied epithelial cells of the corpus luteum consequently are termed lutein cells.[3]

A vascularization of the epithelial layer of the young corpus luteum now occurs by capillaries which enter with the connective-tissue strands from the theca. These press in radial direction into the hypertrophied epithelium of the empty follicle. In the further course of the development of the corpus luteum there occurs a more extensive distribution of connective-tissue septa and blood vessels; until finally small groups of hypertrophied epithelial cells (lutein cells), or even single cells, become surrounded by connective tissue and capillaries. There is thus formed a highly vascular structure which attains a great size (in man 1½—2 cm. in diameter)[4] and always greatly exceeds the size of the follicle previous to its rupture; usually by several times its volume. Recently the corpus luteum has been regarded as a gland of internal secretion whose function however does not yet appear to be completely understood.

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[1] The growth of the connective tissue usually proceeds from cells of the theca interna but may also be due to the outer thecal layer. In animals in which the theca interna is weak all its cells are used. In those with a stouter theca unaltered remnants of it are to be found in the periphery of the corpus luteum. This appears also to be the case in the human ovary.

[2] Lutein, like fat, is soluble in ether etc. and is blackened by osmic acid. It belongs to the so-called lipochromes (p. 17). In man it is found almost as strongly developed as it is, for example, in cattle etc.

[3] The name, lutein cell affords opportunity for a misunderstanding since cells from the theca interna also contain lutein; consequently it is well to use the terms granulosa lutein cells and theca lutein cells. Especially in the case of the human theca interna and in that of many of the larger mammals the highly protoplasmic cells which lie in compact masses in the periphery of the corpus luteum (cf. Pl. 72) are included under this name by certain authors. This practice has little to recommend it and offers a quite erroneous comparison with the true, epithelial lutein cells; although the latter are not difficult to distinguish otherwise than by their origin. In the corpora lutea of the smaller mammals they are completely utilized in the formation of the connective tissue buds, the latter consequently contain none of the so-called theca lutein cells.

[4] In the larger mammals the diameter is decidedly greater.

In many animals more or less marked bleeding occurs, due to the tear made in the ovarian tissues when the follicle ruptures; or the bleeding may occur subsequently to the collapse of the follicular wall. In the human ovary the bleeding appears to be not only constant but quite considerable in amount. A blood clot fills the cavity of the future corpus luteum which at the moment consists only of the collapsed and folded Pl. 72 walls of the ruptured Graafian follicle. While the changes above described are proceeding in the much folded wall, the red blood corpuscles of the coagulum are gradually becoming absorbed. Very commonly haematoidin crystals result from this process. The network of fibrin which remains becomes organized and forms in the center of the coagulum a nucleus of connective tissue which diminishes with progressive hypertrophy of the wall.

A quite unjustifiable distinction is commonly made between the corpus luteum spurium seu menstruationis and the corpus luteum verum seu graviditatis. Always, and in exactly the same way, there is formed a typical corpus luteum from each ruptured follicle, whether the ovum be fertilized or not. However the so-called corpus luteum of menstruation (the name is especially misleading) degenerates much more quickly than does the corpus luteum which is followed by pregnancy.

The degeneration of the corpus luteum proceeds in the first place by a regressive metamorphosis of the epithelial cells; later the framework of connective tissue shrinks. It then forms a kind of scar, the corpus albicans, to be found regularly in every function- Pl. 70, Fig. 2 ing ovary.

The number of primordial follicles and ova has been estimated to be about 36,000 in the human embryo and during the first years of life; recent estimations are even much larger. Naturally of this number only a small fraction come to maturity. Even during childhood the development of vesicular follicles is going on; indeed even in the newborn there are to be found follicles containing liquor. However the transformation of the greater part of the primordial follicles occurs only after puberty, continuing throughout the whole period of the functional activity of the organ. At any stage of its development a follicle may begin to degenerate and this fate overtakes by far the majority of the 36,000 or more. Even follicles which are ready to rupture and whose ova are already undergoing the first maturation division (p. 251) may degenerate completely. This process is known as **follicular atresia,** while the degeneration in the earlier stages of development is best designated as atrophy. Degeneration of the Graafian follicle proceeds first by resorption of the liquor folliculi and a destruction of the epithelium accompanied by the signs of severe karyolysis (p. 29).[1] The theca persists for a time. Indeed it frequently happens in animals that processes of hypertrophy occur within the inner layer of the theca[2] and Pl. 72, Fig. 2 apparently the same occasionally takes place in human pregnancy, during which all the ripening follicles atrophy. Last of all the ovum is destroyed; commonly it becomes fragmented and the nuclei of leucocytes which have entered into the fragments may simulate a typical parthenogenetic segmentation. The membrana pellucida (oölemma) is the most resistant structure of all, a remnant of it often representing the last trace of a Graafian follicle which has disintegrated.

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[1] Karyolysis (chromatolysis) may be recognized even in the first stages of the disintegration of the follicle by the presence of numerous masses of chromatin between the epithelial cells. If the follicle is atretic the ovum will contain the first maturation spindle, or a polar body may already have formed and the second maturation spindle be present.

[2] These structures may simulate corpora lutea since the hypertrophied cells of the theca interna also contain lutein (theca lutein cells). Such structures have been appropriately named corpora lutea atretica. But since the large lutein cells with their abundant protoplasm have been derived from the connective-tissue theca their origin is quite different from that of the true corpora lutea. In addition these structures contain in their interior the ovum, or its remains and often fragments of epithelium as well.

The BLOOD VESSELS of the ovary enter at the hilum and are extremely numerous. They run rather spiral courses within the organ and form dense capillary networks in the theca interna of the follicles and around the clusters of ova. The veins form plexus-like expansions within the medulla and in the region of the hilum pass into the pampiniform plexus. The LYMPHATIC VESSELS have extremely thin walls and lie chiefly in the medulla; in the cortex they are found mostly in the theca externa of the Graafian follicles and of the corpora lutea. Non-medullated, sympathetic nerve fibers enter with the arteries at the hilum and are distributed chiefly as vaso-motor nerves to the walls of the arteries. To some extent they supply the Graafian follicles but do not appear to reach the epithelium. It is doubtful whether medullated, cerebrospinal fibers are present.

The appendages of the female reproductive organs lying in the broad ligament (epoöphoron and paroöphoron) are narrow tubules lined with columnar or ciliated epithelium. The tissue of the medulla passes over without demarcation into that of the broad ligament. As a result there are to be found, exceptionally in the human broad ligament, but constantly in that of many animals, cords of epithelial-like cells which in both situations are given the name of MEDULLARY CORDS.

2. The Ducts of the Female Reproductive Organs

These are the oviduct, the uterus and the vagina.

The **oviduct,** *tuba uterina*, consists of a mucous membrane which is thin in the uterine
Pl. 73 portion of the tube but which becomes thicker and considerably folded in the isthmus; while in the ampulla it reaches a great thickness and forms much branched longitudinal folds. These folds are covered by a simple cubical or columnar epithelium[1] furnished with cilia which produce a current moving towards the uterus. The mucous membrana is rich in connective-tissue cells. Mast cells and wandering cells are present and lymph cells are numerous in the uterine portion of the tube. Collagenous fibers are infrequent and neither elastic fibers nor glands are to be found in the mucous coat.

The folds of the mucous membrane by reason of their length and the abundance of their branching cause great variations in the form of the lumen of the oviduct. In the ampulla and neighboring parts a true central lumen is absent because the long and branching folds extend to the axis of the lumen, so that only a labyrinthine system of clefts is recognizable in place of a lumen. Not until the isthmus is reached does a small central lumen gradually become recognizable.

In addition to the mucous membrane, the wall of the oviduct consists only of muscular and serous coats. No trace of a tunica submucosa is to be found. The MUSCULAR COAT consists of a well developed inner layer of circular muscle[2] which lies close to the mucous membrane and of an outer layer of longitudinal muscle which is much less compact. These two layers are separated by connective tissue containing the larger blood vessels, the large branches of the veins being most conspicuous. The individual bundles Pl. 73, Figs. 1, 3, 4 of the muscular layers are also distinctly separated by strands of connective tissue.

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[1] Nuclei with only a small amount of deeply stained protoplasm are to be found between the ciliated
Pl. 73, Fig. 2 columnar cells and show all stages of being extruded from the epithelium. These appearances are to be
Pl. 3, Fig. 11 seen quite regularly in the human oviduct and in still greater numbers in the oviducts of many animals and are caused by epithelial cells undergoing destruction. Non-ciliated cells containing granules are to be observed; these are secreting cells which in many animals are clearly secreting mucous. Towards the uterus the epithelium becomes gradually, but not greatly, diminished in thickness.

[2] In the outer part of this layer the fibers form bundles which are more and more loosely arranged and which cross one another at acute angles.

The longitudinal muscle of the oviduct lies immediately beneath the serous coat and is continued into the adjacent part of the broad ligament (mesosalpinx) in which it gradually dies away. It thus forms a contrast to the longitudinal muscle of the intestine, ureter, vas deferens etc. in not being an entirely self-contained layer of muscle, a fact which is explained by the manner of its development. It is really a musculature of the broad ligament, while the circular muscle of the oviduct represents the musculature of the Müllerian duct from which both oviduct and uterus are developed. Consequently the same relations hold for the musculature of the uterus; although in the human uterus they are much less obvious than in the uteri of most mammals. These different origins of the two muscular layers explain not only the peculiar arrangement of the longitudinal muscle but also the fact that while in the intestine the chief blood vessels lie beneath the serous coat, in the uterus they lie between the two muscular layers.

The *tunica serosa* of the oviduct shows no peculiarities. It is intimately connected with the longitudinal muscle and is covered by the flat peritoneal epithelium. The fimbria of the infundibulum show a structure similar to that of the oviduct and particularly to that of the ampulla. They have a covering of simple, cubical, ciliated epithelium which is directly continuous with the serous epithelium of the peritoneal cavity. They contain a surprisingly large number of blood vessels of remarkably large diameter.

The larger branches of the BLOOD VESSELS of the oviduct lie between the two muscular layers, surrounded by abundant connective tissue which passes into the tissue of the mesosalpinx. The finer branches penetrate the circular muscle and thus reach the mucous membrane. The course of the LYMPHATIC VESSELS is not so well known. Those which lie in the broad folds of the ampulla and in the fimbria are exceptionally wide lymphatic vessels which resemble the axial lacteals of the intestinal villi. As far as is known the NERVES of the oviduct terminate either in the musculature or in the tunica propria.

The **uterus,** *uterus*, shows in its wall, the same layers as does the oviduct, *i. e.* after Pl. 74 the thick mucous membrane with its numerous glands there follows immediately the muscular coat and after this the serous coat; although the latter is not everywhere present (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II). The mucous coat in the adult is about 1—1.25 mm. thick and is covered by a simple, columnar, ciliated epithelium which is continuous with the similar epithelium of the oviduct, but is decidedly thicker. While the epithelium of the oviduct has only a thickness of 15—18 μ that of the body of the uterus measures 20—25 μ and in the cervix uteri it attains a thickness of 30—35 μ. The tunica propria consists of connective tissue which contains few fibers but is very rich in cells, among which lymphocytes are even more numerous than they are in the Pl. 74, Figs. 2, 4 oviduct. The nuclei of the connective-tissue cells stand so close together as to give to the tunica propria almost the appearance of diffuse adenoid tissue. The few delicate connective-tissue fibers that are present are much interwoven.

Within the mucous membrane are to be found numerous tubular glands, *glandulae uterinae*, which traverse its entire thickness and usually are quite tortuous; their ends Pl. 74, Fig. 2 may be either undivided or forked. They are not set particularly close together but a considerable amount of tunica propria lies between the individual glands. Their diameter remains the same throughout their entire length and they are lined by ciliated epithelium similar to that of the surface of the mucous membrane; on which account they have been Pl. 74, Fig. 3 considered as crypts rather than as true glands. However it is certain that in many mammals the glands produce a secretion. The cells of the glands are shorter than those of the epithelium of the inner surface of the uterus. The base of many of the glands extends even to the muscular layer. Apart from its somewhat greater thickness the mucous mem- Pl. 74, Figs. 5—

brane of the cervix is distinguished from that of the body by differences in the epithelium and glands. The epithelium increases in thickness, becoming high columnar in the cervix; it may lose its cilia, indeed this is the rule in the lower part of the cervix uteri. The glands are less abundant than in the body of the uterus and are more irregular in form, in particular they are more branched and frequently are provided with lateral pockets; on the whole they are decidedly more bulky. In place of the ciliated epithelium of the glands of the body of the uterus, there appears in the glands of the cervix a columnar epithelium which secretes mucus, particularly in the pockets[1] above mentioned. The epithelium of the surface may also form a secretion.

The description given above, as far as it applies to the body of the uterus, is characteristic of the mucous membrane in the interval between two menstrual periods; at which time in most mammals its epithelium is found to lack cilia here and there, or even over extensive areas. The same is frequently the case with the human uterus, the extent of the loss of cilia varying greatly in individuals. During menstruation and for a short Pl. 74. Fig. 4 while before and after the picture of the (pre-menstrual or post-menstrual) uterine mucous membrane changes. In this connection it must be borne in mind that menstruation by no means coincides with ovulation but follows it and is to be regarded as a degenerative process which prepares the uterine mucous membrane for the implantation of the ovum. The mucous membrane, which at the time of ovulation was very hyperaemic, no longer discharges the blood in its overfilled vessels in the ordinary manner, but no inconsiderable part of the blood breaks through the superficial vessels beneath the epithelium and forms sub-epithelial haemorrhages. Here and there the epithelium becomes stripped off and the tissue beneath filled with red blood corpuscles which lie free in the tunica propria. There are thus produced superficial bleeding areas.

The glands also show changes during menstruation. In the pre-menstrual stage they are remarkably wide, particularly at their blind ends. While they, like the entire mucous membrane, suffer at the height of the menstrual phenomena they return again to a medium size when menstruation has ceased. At the same time the denuded surfaces are again covered by epithelium and the mucous membrane slowly assumes the characteristics which it shows during the inter-menstrum. The epithelium during the menstrual period is just as variable as it is during the intermenstruum. It appears as though the number of ciliated cells in the epithelium of the surface increases in the pre-menstrual period. This cycle of phenomena occurs only in the mucous membrane of the body of the uterus.

Pl. 74. Fig. 2 The mucous membrane of both the body and the cervix of the uterus rests directly upon the muscular coat. There is no trace even of a submucous coat to be found.

The MUSCULAR COAT of the uterus, *tunica muscularis uteri*, shows a complicated arrangement of layers since the strands of fibers are interwoven in the most varied directions. Pl. 74. Fig. 1 A subdivision into separate layers[2] consequently is scarcely possible because there are no bars of connective tissue to be found marking off the individual layers. The greater part of the muscle is arranged in a circular or approximately circular direction. Pl. 74. Fig. 1 Longitudinal strands of fibers are to be found chiefly in the form of a weak "submucous" layer[1] close beneath the mucous membrane and as a weak subserous strand of fibers beneath the peritoneal covering of the anterior and posterior walls. This latter layer corresponds to the longitudinal musculature of the oviduct which it resembles in passing into the adjacent part of the broad ligament. In the region of the cervix the external longitudinal muscle becomes somewhat stronger than the inner longitudinal layer and elastic fibers are present quite abundantly throughout the muscle. Frequently considerable quantities of connective tissue are to be found between the muscular layers, particularly around the blood vessels.

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[1] Marked accumulations of mucus in these have received the name of ovula Nabothi.

[2] There may be distinguished a stratum submucosum, stratum vasculare, stratum supravasculare and stratum subserosum. The inclusion in the musculature itself of the larger blood vessels which in the simply formed uteri of many mammals lie between the circular and longitudinal layers, just as they do in the human oviduct, is brought about gradually in the succession of mammalian types by the appearance of oblique muscular strands connecting the chief layers.

The tunica serosa resembles that of the oviduct and is quite firmly united to the subserous muscular layer.

The blood vessels of the uterus are very abundant. Their chief distribution occurs within the middle layers of the muscular coat which, because of the great abundance of the vessels and particularly of the wide veins, has received the name "stratum vasculare". The arterial branches often show marked loops within the muscular coat, from which the mucous coat receives vessels ending in a close, superficial, capillary network. The lymphatic vessels are equally abundant and form three plexuses, one in the mucous coat, a second within the muscle and a superficial plexus beneath the serous coat. The numerous nerves of the uterus are partly medullated and partly non-medullated and show small sympathetic ganglia in the so-called parametrium *i. e.* in the connective tissue lateral to the pars supravaginalis cervicis uteri. Within the wall of the uterus itself no ganglion cells are to be found. The fibers finally lose their medulla and branch, partly within the muscle, partly in the mucous membrane. The most delicate fibers have intraepithelial terminations.

The **vagina,** *vagina*, consists of mucous membrane, *tunica mucosa*, muscular layer, *tunica muscularis*, and fibrous coat, *tunica adventitia*. The mucous coat bears a very thick stratified pavement epithelium which is continuous with that of the *portio vaginalis uteri*[2] and in the region of the os externum passes rather abruptly into the ciliated epithelium of the uterus.[3] In many respects the epithelium resembles the epidermis but is distinguished by the occasional presence of giant cells and nuclei and by frequently containing eleidin (p. 297) in its upper layers. The tunica propria forms papillae which penetrate quite deeply into the epithelium and consists of rather loose connective tissue which contains few cells but has an abundance of fibers. Its deeper layers are extremely rich in elastic fibers which form a fine superficial network and also a second network which is deeper and much coarser.[4] Frequently lymph cells are concentrated and form solitary lymphatic nodules. Small veins are very numerous; glands are almost always lacking. Only in the uppermost part of the vagina are there occasionally to be found scattered

Pl. 75, Figs. 1—3

Pl. 75, Fig. 3

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[1] Indications of this submucous layer are also present in the oviduct.

[2] In this situation the epithelium is decidely thinner than on the vaginal wall proper and papilla are altogether lacking or are merely indicated.

[3] The boundary between the ciliated epithelium and the stratified pavement epithelium is rather variable. Usually in multiparae the pavement epithelium has extended even into the lower part of the cervix uteri; while on the other hand it may happen that some of the portio vaginalis external to the os uteri is covered by ciliated or by columnar epithelium.

[4] During pregnancy the connective tissue of the vaginal tunica propria becomes markedly thickened, distinct clefts form between the bundles and there results a loosening up of the network of elastic fibers. These phenomena are connected with an hypertrophy of the muscle and with a great increase in the diameter of the vessels, particularly of the veins which attain from three to five times their previous size.

glands of the same structure as the glands of the cervix uteri. There is no true tunica submucosa, the mucous membrane passing without sharp demarcation into the muscular coat. Pl. 75, Fig. 1 The latter consists of rather irregularly arranged bundles of smooth fibers; inner circular and outer longitudinal layers occasionally may be distinguished. However as a rule the muscle bundles are quite scattered, have a longitudinal direction and pass insensibly into the outer fibrous layer. The adventitia consists of connective tissue which in parts is dense and contains few elastic fibers, while in other parts it is loose and the elastic fibers are abundant.

The vaginal mucus has an acid reaction and since glands are lacking can be derived only from the epithelium of the surface[1] itself unless it is assumed to be the secretion of the cervical glands of the uterus. In addition to leucocytes and epithelium which has been shed the mucus frequently contains an infusorian (Trichomonas vaginalis).

As to the BLOOD VESSELS of the vagina, the arteries show no peculiarities; while the veins of the mucous coat are very strongly developed and empty into the plexus uterovaginalis which lies partly in the tunica adventitia of the organ. The NERVES resemble those of the uterus. They are present in abundance in the outer fibrous layer and many nerve cells are to be found along their course.

Lateral to the cervix uteri and the upper part of the vagina there is found almost regularly in the newborn and occasionally in later life, a narrow duct formed of columnar epithelium, the so-called duct of Gärtner. It is the remains of the duct of the mesonephros (Wolffian duct, see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. II).

3. The External Female Genitalia

Of the external genitalia the labia majora and labia minora are essentially folds of Pl. 75, Fig. 4 the skin. The *labia minora* have a very great number of quite large sebaceous glands which open on both surfaces. Hairs are absent. The tissue which lies between the glands is a connective tissue which contains many elastic fibers but is free from fat. The epithelium at its surface typically represents the cornified epidermis, while in its deeper layers there are found numerous pigment granules. The *labia majora* on the other hand contain an abundance of adipose tissue. Their external surface presents exactly the characteristics of the skin and contains hairs with sebaceous glands and also sweat glands. The inner surface, turned towards the vestibulum vaginae, resembles a mucous membrane. The *clitoris* is similar in structure to the corpora cavernosa penis. The mucous membrane which covers the glans clitoridis contains genital and tactile corpuscles, while Vater-Pacinian corpuscles are found in the labia majora and tactile corpuscles of Meissner in the long papillae of the labia minora. The *hymen* is a thin connective-tissue partition with a covering of vaginal mucous membrane on its deeper surface and of the mucous membrane of the vestibule on its outer surface.

The *glandulae vestibulares minores* are small mucous glands, $\frac{1}{2}$—1 mm. in size, of tubulo-alveolar type. Their excretory ducts terminate in the neighborhood of the urethral opening. The *glandulae vestibulares majores* (Bartholini) are decidedly larger and correspond in structure to the bulbo-urethral glands of the male.

Appendix I. The Suprarenal Gland, *glandula suprarenalis*[2]

The suprarenal gland, *glandula suprarenalis*, is a peculiar organ of internal secretion Pl. 76, Figs. 1—4 which even macroscopically can be divided into two parts of quite different structure,[1] the epithelial cortex and the chromaffine medulla. The latter is surrounded on all sides by the cortex which usually is many times its bulk; while a connective-tissue capsule encloses the whole organ.

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[1] However if this is indeed the case it would be the only instance in the human body of a secretion being formed by a stratified squamous epithelium.

[2] Although described as an appendage of the urogenital system the relationship is purely regional.

The capsule of the suprarenal gland is formed of connective tissue. It sends into the cortex dense bundles of fibers which form septa between the individual strands of cortical cells. In the deeper parts of the cortex the septa branch and form a network and at the border of cortex and medulla break up into delicate fibers among which elastic elements are unusually abundant. These fibers are continued into the medulla itself.

Pl. 76, Figs. 1, 2

Pl. 76, Fig. 4

Pl. 76, Fig. 3

The epithelial cords of the **cortex,** *substantia corticalis*, form an endocrine cell mass which is of the epithelial corpuscle type. They form cylindrical columns in the broader, middle region of the cortex, that is to say in this region one cell lies flat upon the other. This layer of the cortex is named the *zona fasciculata*. Both towards the surface of the organ and also towards the boundary of the medulla the character of the epithelial cords becomes changed. Beneath the capsule the cords pass into approximately spherical groups of cells *(zona glomerulosa)*, separated from one another by corresponding prolongations of the septa. At the boundary of the medulla the cells form anastomosing cords which are no longer clearly defined since the septa have largely become disorganized. The cords however form an irregular network, the *zona reticularis*. The cells of the suprarenal cortex are about 15—20 μ in diameter. They contain fat droplets[2] which are particularly well marked in the zona reticulata, while in the zona reticularis there are brownish pigment granules which increase in number towards the medulla. The arrangement of cells in rows is thus clearly marked only within the zona fasciculata, the cords of which are usually composed of two or three rows of cells. The cells of the zona glomerulosa are smaller and usually are irregularly polyhedral; more rarely they are approximately columnar. The cells of the zona reticularis are distinguished by the great affinity of their protoplasm for acid aniline dyes. Their content of pigment granules becomes greater as age increases. Between the cell cords of this zone there lie numerous capillaries which form a network of small meshes.

Pl. 76, Figs. 1—3

The **medulla** of the suprarenal gland, *substantia medullaris*, consists essentially of irregular, anastomosing cords or chains of chromaffine cells. These cells are of an irregular polyhedral or long columnar[3] form and measure about 20—30 μ in diameter. The cords surround enlarged capillaries, usually of lacunar form, which are bounded merely by endothelium. Each medullary cell, which in general is of an elongated shape, is in contact with a blood capillary by its two smaller surfaces while its broader surfaces are in contact with the neighboring cells of the chain.

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[1] That the cortex and medulla of the suprarenal (adrenal) gland have nothing in common, is seen best in the lower vertebrates in which two kinds of adrenal gland are present: 1. adrenal organs of cortical material and 2. interrenal organs of medulla. Even in man there are frequently found small accessory suprarenal bodies consisting merely of cortex; *e. g.* in the broad ligament of the female and in the neighborhood of the seminal vesicle of the male.

Pl. 76, Fig. 4

[2] These inclusions are lipoids and determine the intense yellow color of the suprarenal cortex. The protoplasm of the cells appears extremely vacuolated because of the large lipoid droplets. The cells of the zona glomerulosa have fine granular inclusions.

[3] The finely granular cells shrink slightly from the action of fixing reagents and then appear to be serrated.

The cells of the medulla have relatively small nuclei which contain little chromatin. Their protoplasm contains fine granules which are colored brown by salts of chromic acid and consequently are said to be of chromaffine or phaeochrome substance. This substance, which contains chemically the extremely active principle adrenalin, passes from the cells into the wide capillaries which they enclose and by the aid of salts of chromium may even be demonstrated in the lumen of the capillaries.

The medulla of the suprarenal gland is not the only structure which is formed from **chromaffine** cells although it does represent the largest accumulation of such cells. These cells according to their origin are derivatives of the anlagen of the sympathetic nervous system and have received the name of sympathetic paraganglia. In addition to forming the medulla of the suprarenal gland they are found in quantity only in the so-called carotid gland (see below); elsewhere small groups of these cells together with small, true, sympathetic ganglia are found in the neighborhood of the male and female reproductive organs, partly as isolated masses and partly within the ganglia. Although derivatives of anlagen of the nervous system they have no nervous function, nor do they assume the shape etc. of nerve cells but remain of epithelioid form. Phaeochrome tissue is said to be present in the hilum of the ovary and in the connective tissue of the mesovarium and of the mesosalpinx as rounded or elongated cells of epithelioid appearance with distinct cell boundaries and eccentric nuclei, poor in chromatin. Such cells are to be found especially along the course of the nerve trunks.

The medulla of the suprarenal gland contains a great abundance of non-medullated nerve fibers and nerve trunks, also oft true nerve cells, singly or in groups. Large venous
Pl. 76, Fig. 2 branches are also present in which there may be observed peculiar local thickenings of the wall formed of connective tissue and muscle.

The BLOOD VESSELS of the suprarenal gland are very abundant. The small arterial branches run in the septa between the epithelial cords and there form the cortical capillary plexus, the meshes of which are long and in the zona reticularis become quite narrow. Other arteries pass without branching into the medulla and supply the wide capillaries. The larger veins lie exclusively in the medulla and contain much muscle in their walls, in particular, longitudinal strands are numerous in the tunica adventitia.

The NERVES of the suprarenal gland are very abundant in proportion to the size of the organ. They are without exception branches from the sympathetic system and consist for the most part of non-medullated fibers. They form plexuses in the cortex, especially in the zona reticularis, but branch most abundantly in the medulla where they surround each individual medullary cell with a basketlike network.

Appendix 2. The Carotid Gland, *glomus caroticum*

The so-called carotid gland, *glomus* (paraganglion) *caroticum*, next to the medulla of the suprarenal gland is the largest mass of chromaffine material in the human body.
Pl. 76, Fig. 5 This small structure, situated at the bifurcation of the common carotid artery, does not however consist of a single compact mass of tissue but is formed of a few separate bodies of larger or smaller size which consist of chromaffine cells. The connective tissue septa between these bodies contain many small blood vessels and nerve trunks, the latter consisting of non-medullated fibers. The numerous vessels enter into and vascularize the masses of phaeochrome cells.

X. The Organ of Vision

The organ of vision — the visual apparatus in the widest sense of the word — is divisible into the eyeball, bulbus oculi, and its accessory structures, namely, 1. the eyelids and the conjunctiva, 2. the lachrymal apparatus, 3. the mechanism for movement of the eyeball (muscles, tendons, fasciae). Microscopically the latter show no peculiarities of structure and will not, in this connection, receive special description.

The Eyeball, *bulbus oculi*

The eyeball is a rather regular, hollow, thin-walled sphere the greater part of whose contents are fluid or almost fluid. Forming the anterior surface of the sphere is the cornea — a segment of a somewhat smaller sphere. Pls. 77—82

The wall of the sphere is formed of three coats, tunica externa s. fibrosa (= sclera + cornea), tunica media s. vasculosa (uvea + chorioidea + corpus ciliare + iris), tunica interna (retina + pigmentary epithelium). Only one coat, the tunica externa, is represented in the cornea.

The cavity of the eyeball is subdivided into a larger posterior and a smaller anterior part by a septum, the iris, which is a special part of the middle coat. An opening in the center of the iris, the pupil, is covered posteriorly by a biconvex body, the lens, lying in the posterior part of the cavity.

By far the greater part of the space behind the iris is filled with the vitreous humor, the anterior surface of which is thickened to form the zonula ciliaris, the boundary of the posterior chamber of the eye. The space between iris and cornea is called the anterior chamber of the eye and contains a fluid. The optic nerve enters at the posterior surface of the eyeball, nearer to the nasal than to the temporal side. (See Sobotta McMurrich, Atlas of Human Anatomy, Vol. III.)

1. The External Coat of the Eyeball, Sclerotic Coat, *tunica fibrosa oculi (externa bulbi)*

The cornea, the anterior transparent portion of the external coat of the eyeball, consists chiefly of a variety of fibrous connective tissue which is formed of peculiar flattened bundles.[1] Its anterior surface is covered by epithelium, all else is connective tissue. The thickness of the cornea varies from 0.8 mm. at its center to 1.1 mm. at its margin. Pl. 77, Fig. 1 Pl. 78, Figs. 2, 3

For purely descriptive purposes five layers are generally distinguished in the cornea. From the anterior surface inward these are 1. the epithelium, 2. the anterior elastic membrane (Bowman's membrane, lamina elastica anterior), 3. the substantia propria corneae, 4. the posterior elastic membrane (Descemet's membrane, lamina elastica posterior), 5. the endothelium of the anterior chamber of the eye.

The EPITHELIUM of the cornea passes at its border directly into the epithelium of the conjunctiva. Like the latter, it is a very simply constructed, stratified squamous epithelium (p. 35), but has no papillae and but few layers of flat cells. Upon the lower columnar layer[2] there follow as a rule two layers of round and two layers of flat cells. The epithelium at the center of the cornea measures about 50 μ in thickness; near the margin it is somewhat thicker, about 80 μ. Occasionally wandering cells are found in the epithelium. Pl. 78, Fig. 3

The *anterior elastic membrane* is very distinct in man[3] and has a thickness of 10 to 12 μ. It appears almost homogeneous and free from cells, but is only a specially modified layer of the substantia propria into which it passes without demarcation. It is not elastic but entirely of the nature of collagenous connective tissue like the propria itself, but less fibrillar. The epithelium rests upon it, separated only by a quite thin hyaline layer, probably of epithelial origin.

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[1] The collagen obtained from the cornea by boiling differs somewhat from that of ordinary connective tissue.

[2] The nuclei of the columnar cells lie regularly in the upper part of the cell. Quite slender, footlike processes from the cells of the layer above reach between the columnar cells to the basement membrane.

[3] In most mammals Bowman's membrane is weak, or not developed at all.

The *substantia propria corneae* forms the chief mass of the cornea, about $^{9}/_{10}$ of the Pl. 78, Fig. 2 total thickness. It consists of fibrous connective tissue of special, and in part very complicated, structure. Its bundles are cemented together so as to form numerous thin, flat lamellae which lie closely one upon another but are distinctly separate.[1] The lamellae always lie parallel to the surface of the cornea and within each lamella all the fibers are parallel; although their direction differs in different lamellae.[2] Between each two lamellae is a small quantity of cement and the corneal cells, the so-called corneal corpuscles, Pl. 6, Fig. 6 or fixed cells of the cornea.[3] These are extremely flat, connective-tissue cells with long, flat, branched processes by means of which they connect with neighboring cells and thus — at least in many animals — form very regular rectangular meshes.[4] They lie in spaces of corresponding form which are joined to one another by fine canals (corneal Pl. 6, Fig. 7 canals) containing the processes of the cells. The cells fill the spaces so completely that canals and spaces are to be regarded only as a system to contain the pericellular fluid.

The human *lamina elastica posterior* is a thin, hyaline membrane, 6—10 μ in thick-Pl. 8, Fig. 5, ness and entirely structureless. It may be isolated from its contacts and in contrast to the Pl. 36, Fig. 1 anterior elastic membrane is perhaps related to elastic tissue.[5] Its margin is thickened Pl. 78, Fig. 2 and terminates at the angle of the iris by splitting up into the tissue of the ligamentum pectinatum iridis (p. 267); but neither here nor in any other part is it to be considered true elastic tissue.

The corneal endothelium is the portion of the endothelial lining of the anterior chamber of the eye which covers the posterior surface of the cornea. It is — like every endothelium — strictly of but one layer of cells which are flattened, hexagonal, and quite epithelial Pl. 8, Figs. 5, 6 in appearance, with rounded or polymorphous nuclei.[6] They form a continuous layer like an epithelium although the connective-tissue origin of the cells is demonstrable beyond question (p. 94).

The **sclera** is composed chiefly of dense connective-tissue bundles woven together in Pl. 78, Fig. 1 meridional,[7] equatorial and various other directions. In contrast to the similar bundles Pl. 6, Fig. 2 of the cornea they contain both stout and slender elastic fibers, the latter predominating. In the anterior portion the meridional bundles are most numerous, in the posterior part those which have a circular direction. The former are more numerous in the inner layers of the coat than in the outer and particularly so at the insertions of the muscles of the eyeball and at the entrance of the optic nerve. In general the thicker, posterior part of the sclera is richer in elastic fibers than the anterior part. The sclera contains flat, connective-tissue cells but in smaller numbers than does the cornea. They resemble tendon cells more than corneal cells and like true tendon cells often show furrows which represent the impressions of the adjacent bundles of connective tissue.

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[1] Special limiting membranes appear to be present at the surfaces of the individual lamellae.

[2] Beside the fibers of the bundles which form the lamellae there are finer ones, fibrae arciformes, which penetrate the individual lamellae and bind them together. The latter are especially numerous in the anterior part of the cornea where they unite Bowman's membrane to the anterior lamellae. In the lamellae themselves there occur a few fine fibers different from the rest and considered by many to be elastic fibers, but which may be pre-elastic fibers (p. 62).

[3] So called because wandering cells are also present in the cornea.

[4] In contrast to their condition in the frog and also in the rabbit these cells in man do not show this regular and rectangular branching; but are blunt and irregularly formed, with a few stout processes that anastomose irregularly. However even in man the cells as a whole form an extended network throughout the entire cornea.

[5] It probably arises from the endothelium on its posterior surface and is perhaps formed of pre-elastic tissue (p. 62).

[6] In many mammals the nuclei are kidney or horse-shoe shaped and contain in the concavity the centrosome in the form of a diplosome. Various cell inclusions have been observed in the corneal endothelium.

[7] The meridional direction in the anterior part of the coat is determined by the insertion of the "recti" muscles of the eyeball.

The inner layer of the sclera, next to the middle coat of the eyeball, differs somewhat in structure from the above. It is formed of a looser connective tissue containing many elastic fibers and numerous rounded pigment cells with but few flattened branches (pigmented connective-tissue cells) and also flat endothelium-like[1] cells free from pigment. This layer is known as the *lamina suprachorioidea (lam. fusca)*, but according to its structure it belongs to the chorioidea rather than to the sclera (p. 264). The pigment in Pl. 78, Fig 4
these cells is melanin (p. 15) and usually is very abundant.

The sclera shows a peculiar formation where it is penetrated by the optic nerve; the latter does not enter through a simple opening of corresponding form and diameter Pl. 77, Fig 1
as is the case where it penetrates the chorioidea, but the individual bundles penetrate Pl. 82, Fig 3
the scleral tissue separately, each receiving from it a covering rich in elastic fibers. The numerous perforations produce in the sclera a sievelike area named the LAMINA CRIBROSA SCLERAE.

The thickness of the sclera in the posterior part of the eyeball is considerable, about 1 mm.; while anteriorly it becomes thinner being only 0.3 mm. at the equator, but increases again to 0. 6 mm. near the insertions of the eye muscles. Microscopically its tissue passes into the cornea without sharp delimitation at the so-called corneal groove. The blood vessels cease at this point and the arrangement of the connective bundles and cells becomes different; at the same time fibers of the sclera can be followed far into the cornea.

The tunica externa bulbi, like all fibrous tissue, is poor in BLOOD VESSELS; the cornea lacks them completely. In the region of the transition from the sclera to the cornea and near the anterior chamber there is a ring-shaped vein, often plexiform, running parallel Pl. 77, Fig. 2
to the border of the cornea, the *sinus venosus sclerae* or canal of Schlemm. There are no Pl. 79, Fig. 2
lymphatic vessels in the tunica externa, nor as far as is known in the entire eyeball.

NERVES are few in the sclera proper but abundant in the cornea and are branches of the ciliary nerves. The fibers of the numerous nerves which enter the cornea at once lose their medullary sheath notwithstanding their cerebro-spinal origin, for the medulla would interfere with the transparency of the organ. The cornea is peculiar in the formation of its nerve plexuses; the first of these is in the deeper layers of the substantia propria. Some fibers go directly from it to the cells of the propria, others penetrate perpendicularly Pl. 39, Fig 1
through the lamellae and form another plexus beneath the anterior elastic (Bowman's) membrane. Branches from this plexus traverse the membrane to reach the base of the epithelium and form there the subepithelial plexus. From the latter many fibers enter the epithelium itself and form numerous free, intra-epithelial endings. Special terminations are also present in the substantia propria.

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[1] On the outer surface of the sclera and on the tissue of the space of Tenon, the so-called loose, episcleral tissue (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III), there is present an endothelium-like layer of flat connective-tissue cells. Few pigment cells are to be found in the sclera, but they are more abundant among the pigmented races than in Caucasians. They are most numerous near the entrance of the optic nerve and at the scleral swelling *i. e.* the slight ringlike thickening of the anterior part of the sclera over the site of the ciliary muscle.

As they pass through the sclera, the ciliary nerves give off fine branches which partly are nerves to the blood vessels, and partly form free endings in the coat itself. Usually they lie in the inner layer of the coat and consist of medullated fibers.

Pl. 77
Pl. 78, Figs. 1, 4
Pl. 79, Figs. 1—4
Pl. 80, Fig. 5

2. The Middle Coat of the Eyeball, Chorioid Coat, *tunica vasculosa oculi* (*tunica media bulbi, uvea*)

The middle coat of the eyeball, tunica vasculosa (or better vasculoso-musculosa) also named the **uvea,** is uncommonly rich in vessels and contains upon the whole all the essential vessels of the eye.[1] It is subdivided into chorioidea, corpus ciliare and iris.

Pl. 78, Fig. 1
Pl. 79, Fig. 1

The **chorioid coat,** *chorioidea*, the posterior portion of the middle coat of the eyeball is a highly vascular, pigmented, connective-tissue coat, in the chief part of which the two principal characteristic layers can be distinguished by the disposition of their blood vessels. The inner of the two, the *lamina choriocapillaris*, serves essentially for the nourishment of the adjacent retina[2] and is formed of wide capillaries placed close together. The outer, the chief layer of the coat, the *lamina vasculosa* (chorioidea propria) contains the larger arteries and veins. The vessels of the chorioidea, apart from the capillaries, lie embedded in a connective tissue stroma which is quite rich in elastic fibers but poor in the collagenous variety and which contains large numbers of pigmented cells.[3] Stout strands of fibrillar connective tissue are present only in the neighborhood of the larger vessels. The veins of the chorioidea are entirely devoid of muscle; even the arteries contain only scattered bundles of circular muscle fibers, all of whose nuclei often lie on the same side of the lumen of the vessel. In the choriocapillaris, capillary lies by capillary with almost no tissue intervening, the whole forming an exceedingly fine meshed plexus which is strictly of but one layer of capillaries. Between the two chief layers of the chorioidea there lies a kind of boundary layer, the STRATUM ELASTICUM SUBCAPILLARE, formed of elastic fibers and flat cells. The choriocapillaris is separated from the tunica interna bulbi by a layer of finely woven elastic fibers, the STRATUM ELASTICUM SUPRACAPILLARE, followed by a fine structureless membrane not more than $\frac{1}{2}\mu$ thick, and named the *lamina basalis chorioideae*.[4] This latter is not of elastic nature and probably does not belong to the chorioidea but to the pigmentary epithelium of the retina and is an epithelial hyaline membrane. The suprachorioidea or *lamina fusca sclerae* consists of loose, pigmented connective tissue and contains both rounded and flattened connective-tissue cells which are especially rich in pigment and show small numbers of anastomosing processes. If the sclera and chorioidea are separated the lamina fusca clings partly to the outer surface of the latter (p. 263).

Pl. 78, Fig. 4

In the chorioidea of most domestic animals there is a structure of metallic lustre, the *tapetum (lucidum)* which is entirely wanting in the human eye. It consists either of wavy bundles of connective-tissue fibers (tapetum fibrosum) as in ruminants and perissodactyles, or of several layers of flat cells containing fine crystals (tapetum cellulosum) as in the carnivora. The position of the tapetum is in the boundary layer between choriocapillaris and lamina vascularis.

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[1] In addition to the vessels of the middle coat, there are in the eyeball only those in the inner layers of the retina and a few in the sclera; all the remaining parts (cornea, lens, vitreous humor and zonula ciliaris) are without vessels.

[2] The vessels lying in the retina itself nourish only the inner layers of the coat (p. 277).

[3] Flat, unpigmented, endothelial-like cells also occur. The choriocapillaris is free from pigment.

[4] As a rule the two layers together measure $1-1\frac{1}{2}\mu$ and are known as Bruch's membrane or the hyaline membrane of the chorioidea. As usually stained they appear to be a single layer and earlier were considered as such. The choriocapillaris is wanting in the region of the orbiculus ciliaris.

Pl. 77, Fig. 2
Pl. 79, Fig. 2
Pl. 81, Fig. 3

The ciliary body, *corpus ciliare*, consists of two principal parts: 1. a ring-shaped muscle, the MUSCLE OF ACCOMODATION, *musc. ciliaris*, which lies close to the adjacent sclera and 2. the *processus ciliares*, 70 elevations in the form of meridionally directed folds which project toward the vitreous humor.[1] The ciliary body also includes the *orbiculus ciliaris*, an area free from folds which lies behind the ring of ciliary processes or corona ciliaris.

The CILIARY PROCESSES are essentially ridgelike elevations of the fibro-elastic basis of the ciliary body and are distinguished by an extreme richness in blood vessels which form capillary loops crowded together in the processes. The ciliary processes are covered by both lamellae of the optic cup, the outer is the pigmentary epithelium, the inner is the pars ciliaris retinae and consists of a cubical or columnar, simple, unpigmented epithelium. The former (p. 268) shows here a peculiarity in that its cells, particularly those on the crests of the ridges, have little pigment; consequently in lightly pigmented individuals these cells are entirely free from pigment, an exceptional thing in the pigmentary epithelium.

Pl. 77, Fig. 2
Pl. 78, Fig. 4
Pl. 79, Figs. 2, 4
Pl. 81, Fig. 3

The ciliary muscle consists throughout of smooth muscle fibers[2] arranged in three directions. The outer fibers lying next the sclera are directed meridionally and form the longest portion of the muscle (tensor chorioideae — Brücke), extending from the wall of the sinus venosus sclerae (p. 263) and the scleral swelling to the anterior part of the chorioidea, or at least to the posterior part of the orbiculus ciliaris. Next internally are the bundles of radial fibers *i. e.* those fibers which run from near the base of the iris in a general radial direction toward the center of the eyeball. They show distinctly a loosely interwoven arrangement and in part are deflected into a circular direction.[3] The most internal fibers of the muscle run in a strictly circular direction; their number varies and is often quite small[4] (equatorial portion — Müller). The meridional portion alone is a compact layer penetrated only by scattered, fine elastic fibers; the radial and circular bundles are separated by considerable quantities of the connective tissue of the ciliary body.

The connective tissue of the ciliary body resembles that of the chorioidea; it contains both collagenous and elastic fibers and branched, pigmented connective tissue cells, although the latter are often few in number. Toward the tunica interna bulbi (pars ciliaris retinae) the connective tissue of the ciliary processes terminates in a continuation of the lamina basalis chorioideae.[5]

Pl. 77
Pl. 79, Figs. 2, 3
Pl. 81, Figs. 3, 5

In the **iris** three, or sometimes four, layers are generally recognized: 1. the endothelium of the anterior chamber of the eye covering the anterior surface of the iris, 2. the stratum proprium iridis, 3. the posterior limiting membrane, Bruch's membrane, 4. the pigmentary layer of the iris. Layers 3 and 4 belong properly to the tunica interna oculi.

Thus the iris really consists of two quite different coats of the eyeball; the same is true for the ciliary body, only in this case it is not so obvious as in the iris. A distinction must be made between the anterior connective tissue layers of the iris which alone represent the middle coat of the eyeball and its posterior epithelial covering belonging to the retina. Both lamellae of the optic cup are represented in the posterior epithelium of the iris and in this situation both are pigmented (p. 268).

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[1] See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III.

[2] In all mammals. In birds and reptiles the muscle like the rest of the intrinsic muscle of the eye is formed of striated fibers.

[3] Strictly considered the radial parts of the muscle are only strands which are gradually bending from the circular direction into the meridional.

[4] In short-sighted individuals the circular portion is often entirely wanting.

[5] Just here some collagenous connective tissue lies between the elastic part of the membrane and the basement membrane proper. In the region of the ciliary processes the elastic part of the membrane becomes much subdivided.

The ENDOTHELIUM of the anterior surface of the iris is the direct continuation of that of the posterior surface of the cornea; however it is here less regular and epithelium-like in its whole arrangement. It is discontinuous here and there and entirely wanting in the region of the crypts of the iris. Its elements also, especially at the bases of the crypts, are directly connected with the underlying, true connective-tissue cells.

Pl. 79, Figs. 2, 3 The *stratum proprium iridis* falls into two subdividions, the one a reticular or anterior limiting layer formed of closely placed cells[1] and a little collagenous connective tissue, the other a posterior vascular and muscular layer. In addition to numerous blood vessels and in places smooth muscle, the latter contains connective tissue whose cells bear but little pigment in light-colored eyes but are heavily pigmented when the iris is dark. (In the latter case there are present in addition branched, unpigmented cells.) Both the branched and the pigmented cells form networks; a few scattered elastic fibers are present in addition to the collagenous fibers. At the bases of the crypts of the iris this layer often approaches closely the wall of the anterior chamber since not only the endothelium is wanting but often the anterior reticular layer as well. Concerning the so-called "klumpenzellen" see page 269.

Pl. 79, Figs. 2, 3
Pl. 81, Fig. 5 The MUSCLES of the iris are the *musculus dilator pupillae* represented by the posterior basal layer and the *musculus sphincter pupillae* which, like a ring, surrounds the margin of the pupil, and lies nearer to the posterior than to the anterior surface. Beside the purely circular bundles there are present fine radial bundles which pass into the muscle layer of the dilator; but in man these occur only in small numbers. The sphincter, as well as the dilator, is by development an epithelial muscle since it takes origin from the epithelium of the pupillary margin; a connection which it retains through life.

Pl. 79, Fig. 3
Pl. 81, Fig. 5 The muscle of the dilator pupillae is represented by the posterior limiting layer of the iris, a thin, flat, membrane-like, protoplasmic layer whose muscular character was for a long time unrecognized.[2] Recent investigations have shown that the anterior layer[3] of the reduplicated pigmentary epithelium of the iris (p. 268) is differentiated to form smooth muscle; that the anterior part of the cell, containing little pigment, represents the contractile substance, while the posterior part, rich in pigment, contains the nucleus.

The blood vessels of the human iris have pronouncedly radial courses. As a whole they are devoid of muscle and elastic fibers but have heavy sheaths of connective tissue, possibly pigmented, which are supplied by the stroma of the iris. Concerning the pigment layer of the iris see under the tunica interna oculi.

Pl. 79, Fig. 3
Pl. 81, Fig. 3 The iris is from 0.4 to 0.5 mm. thick. Special structural relations are shown near the **angle of the iris** *i. e.* near the region where the root of the iris emerges from the ciliary body. Here a very intimate union occurs between the outer and the middle coats of the eyeball, the iris sending out connective-tissue processes which, although poorly developed

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[1] These cells form nets and in eyes with dark iris are frequently pigmented, often strongly so, like the cells of the vascular layer.

[2] Consequently this posterior limiting membrane of the iris has been named Bruch's membrane just as in the chorioidea, although it is fundamentally different.

[3] This refers only to the anterior stratum of the pigment layer, the pigmentary epithelium, not to the pars iridica retinae.

in adults, enter into firm union with the posterior basal membrane of the cornea[1] and to some extent even with the posterior layers of the substantia propria corneae. The peculiar network which constitutes the wall of the canal of Schlemm and separates the canal from the anterior chamber (scleral network of the ligamentum pectinatum) represents the only noteworthy remnant of this structure, which, in its entirety, is to be observed only during youth. This structure, rudimentary in man but well developed in most other mammals, is named the *ligamentum pectinatum iridis*.[2] Between the fibers of the ligament are communicating spaces (of Fontana) connected with the anterior chamber of the eye and filled with the aqueous humor. These "spatia anguli iridis" are really found only in the eye of the new-born child in which they are lined by the endothelium of the anterior chamber. In the eye of the adult the uveal portion of the ligamentum pectinatum entirely degenerates. As a result the angle becomes sharply defined, the spaces of Fontana disappear, and only the scleral portion of the "ligament" remains as the peculiar, loose, scleral tissue that separates the sinus venosus sclerae from the anterior chamber. Pl. 81, Fig. 3

The BLOOD VESSELS of the middle coat constitute the vessels of the CILIARY SYSTEM, one of the two vascular systems of the eyeball.[3] The vessels of the chorioidea are principally the arteriae ciliares posteriores breves while the arteriae ciliares posteriores longae and the arteriae ciliares anteriores supply the ciliary body and iris. In the lamina choriocapillaris the vessels are all in one layer and form a network of very small meshes but show no other peculiarity. On the other hand the vessels of the anterior part of the tunica media form at the base of the iris a vascular ring, the circulus (annulus) iridis major, from which proceed the vessels of the ciliary body and the vessels, mostly radial, of the iris. The latter form a circular anastomosis at the margin of the iris, the circulus (annulus) iridis minor.

Apart from the sinus venosus sclerae the large veins of the tunica media, the venae vorticosae, are four in number and lie near the equator of the eyeball. There are no lymphatic vessels anywhere in the eyeball; in their stead perivascular lymph spaces may be present but their existence is questioned.

The nerves of the chorioidea are principally those to the vessels. The motor nerves of the iris and ciliary body are derived from the n. oculomotorius (para-sympathetic part) and from the n. sympatheticus. In the ciliary body they form a plexus containing nerve cells,[4] the plexus gangliosus ciliaris, which consists principally of medullated fibers. The fibers of the iris are also medullated, a point of contrast with those of the cornea (p. 263).

3. The Internal Coat of the Eyeball, *tunica interna oculi (bulbi)*

The tunica interna consists of two principal layers — or better, of two lamellae —, the PIGMENTARY EPITHELIUM, *stratum pigmenti*, and the *retina* proper. They represent the two closely applied lamellae of the secondary optic vesicle or optic cup.

It must be noted that in the fully developed eye of the adult the optic cup is still recognizable as such, its opening coinciding with the pupil. The external lamella is the pigmentary epithelium which is a simple epithelium throughout its whole extent; the internal lamella is the retina. In the posterior part of the wall of the cup the retina developes into nervous tissue and becomes relatively thick (pars optica retinae) while in the anterior part it is a simple epithelium (pars caeca retinae). The internal lamella is unpigmented with the exception of its most anterior part applied to the hinder surface of the iris where it is as deeply pigmented as is the external lamella.

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[1] The basal membrane thus breaks up into fibers at its periphery (p. 262).

[2] The intermuscular connective tissue and elastic fibers of the region of the ciliary muscle and also fibers from the sclera share in the tissue of the ligamentum pectinatum. It is the only place in the eyeball where the outer and middle coats are firmly connected; since throughout its whole extent the chorioidea is easily detached from the sclera.

[3] See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III.

[4] These cells, the number of which is by no means great, may well be solely of sympathetic origin.

The Pigmentary Epithelium, *stratum pigmenti*

Pl. 77
Pl. 78, Figs. 1, 5
Pl. 79, Figs. 1, 3, 4
Pl. 80
Pl. 81, Figs. 1, 4, 5

The pigmentary epithelium, stratum pigmenti, the external lamella of the optic cup, when considered by regions falls into three parts: stratum pigmentum retinae, stratum pigmenti corporis ciliaris, and stratum pigmentum iridis. But this distinction is not merely regional for considerable differences are to be recognized in the microscopical characteristics of the three areas. The whole pigmentary epithelium is alike in that the pigment contained in its cells is an iron-holding pigment known as fuscin (p. 16).

Pl. 80, Fig. 4

The stratum pigmenti retinae is a simple cubical epithelium which lies immediately to the outer side of the layer of the rods and cones. The hexagonal mosaic of its cells appears most distinctly in surface views. Although it is intimately related to the rods and cones it is easily separated from them, while it is relatively firmly attached to Bruch's membrane of the chorioidea (p. 264). Usually the cells contain but ONE nucleus although toward the ora serrata exceptionally large, binucleate cells are present. The position of the nucleus is always in the least pigmented part of the cell, that which is turned toward the chorioidea. The cell boundaries are very distinct since a highly refractive zone, free from pigment, separates the pigmented cell bodies as though it were an intercellular cement.[1] The pigment itself, which preferably fills the part of the cell turned toward the rods and cones, is in the form of short rods or needles which have a thickness of about 1 μ and a length of 3—4 μ. They lie pressed irregularly together in the body of the cell but in strong light they accompany processes of the protoplasm into the spaces between the outer segments of the rods and cones.[2] In the region of the fovea centralis the cells are longer and correspondingly more slender than in the remaining areas of the retina.

Pl. 79, Fig. 4
Pl. 81, Fig. 4

The *stratum pigmenti corporis ciliaris* is essentially the same. The cells are longer, varying from high-cubical to low-columnar. The pigment is relatively more abundant than in the cells of the stratum pigmenti retinae and fills the whole extent of the cells; consequently neither the nucleus nor the cell boundaries are visible, although after decolorizing they may be seen distinctly. In addition the pigment, although it is still fuscin as in the retinal region of the layer, no longer appears in the form of needles but of irregularly rounded particles of varying size. Naturally the cellular processes mentioned above are lacking since the columnar epithelium of the non-visual part of the retina is immediately applied to this surface. The nucleus lies in the center of the cell.

Pl. 78, Fig. 5
Pl. 79, Fig. 4
Pl. 81, Fig. 4

At the ends of the ciliary processes the pigment granules are few or according to circumstances are altogether absent for a distance (p. 265). In the region of the orbiculus ciliaris the pigmentary epithelium is not a uniform layer but sends numerous budlike outgrowths into the connective tissue of the ciliary body where they join to form a network, the so-called reticulum of MÜLLER.[3]

The STRATUM PIGMENTI IRIDIS varies from the above in structure, although it resembles the pigmentary epithelium of the ciliary body in regard to form and arrangement. The cells become again somewhat shorter, flat-cubical, and the cell boundaries and nuclei are obscured by the irregularly rounded particles of pigment. The nuclei lie in the posterior zone of the cell, *i. e.* in the part turned toward the pars iridica retinae, which also contains the greater part of the pigment. The anterior region of the cells is relatively free from pigment though not completely so, but no cell boundaries can be recognized in it; consequently the layer appears to be of syncytial character. In addition after depigmentation this zone of the epithelium displays a distinctly fibrillar structure. This is the so-called DILATOR MEMBRANE formed by the transformation into smooth muscle of part of what otherwise is a typical epithelial lamella. Isolated pigment cells from the epithelium are found very abundantly as irregularly formed elements scattered in the iris near the musculus sphincter pupillae, "klumpenzellen". The pigmentary epithelium of the iris extends to the margin of the pupil, *i.e.* to the margin of the optic cup where it turns back as the pars iridica retinae (p. 276).

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[1] By some authors this cement substance has been termed neurokeratin.

[2] This phototropic migration of pigment may be very clearly demonstrated in the retina of the frog.

[3] This peculiar arrangement of the pigmentary epithelium leads to a firm fixation of the wall of the optic cup and of the inner to the middle coat of the eyeball; as a result the ciliary muscle situated in the latter (p. 265) can act upon the fibers of the zonula (p. 279) which arise from the cells of the pars ciliaris retinae.

Pl. 79, Figs. 2, 3
Pl. 81, Fig. 5

The Retina, *retina*

The *retina* proper falls into two chief parts, the *pars optica* and the *pars caeca*, the latter being again subdivided into the *pars ciliaris* and the *pars iridica retinae*. The pars optica and the pars caeca retinae are separated by a sharp line, the *ora serrata*, which is visible to the unaided eye, and which runs a course that is slightly wavy on the temporal side of the eye and jagged on the nasal side.

a. ***Pars optica retinae***

The structure of the pars optica *retinae* is essentially as follows:[1] considered as to structure and function there are three constituents, the SUPPORTING ELEMENTS, the CEREBRAL LAYER comprising the NERVOUS ELEMENTS in the narrower sense and the NEURO-EPITHELIUM. The supporting elements are very intimately intermingled with the other constituents and are only to be distinguished from them by special methods. Nor do the nervous elements or the neuro-epithelium appear in their perfect form and mutual relations except through the employment of special methods. Examining the retina with the ordinary means of investigation it appears to be composed of a number of concentric layers,[2] from within outward as follows: 1. membrana limitans interna, 2. layer of fibers of the optic nerve, 3. ganglion cell layer, or better, layer of the ganglion of the optic nerve, 4. inner reticular or plexiform layer, 5. inner nuclear layer, 6. outer reticular or plexiform layer, 7. Henle's fiber layer, 8. outer nuclear layer, 9. membrana limitans externa, 10. rods and cones. The limiting membranes 1 and 9 belong entirely to the supporting substance, while layers 2—6 form the cerebral layer and layers 7, 8 and 10 the neuro-epithelium.

Pl. 78, Fig. 1
Pl. 80, Figs. 1—5
Pl. 81, Fig. 1

In describing the structure of the retina the **glial supporting elements** will first be considered. These are the so-called RADIAL FIBERS of MÜLLER, elongated glia cells which extend through almost the entire thickness of the retina. The ordinary methods of staining reveal them as "fibers" running perpendicularly to the retinal surface. Each begins with a conical expanded end or "foot" at the membrana limitans interna. The latter is not an independant membrane but is formed by the firmly united feet of the radial fibers, however it simulates a "membrane" since it easily separates from the fiberlike part of the cells.

Fig. 36

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[1] Since the finer structure of the retina is very complicated and in certain parts not thoroughly understood, this account is restricted to the facts which are most important and well ascertained.

[2] The old classification of the layers is retained because it is still in general use and in spite of its incompleteness cannot be dispensed with at present, at least not until new terms are introduced and generally accepted.

Above the foot there follows the narrower, more fiberlike part of the cell which penetrates in turn the layer of nerve fibers, the layer of ganglion cells and the inner reticular layer. In the inner nuclear layer the fiber grows somewhat broader and shows a rounded or elliptical nucleus. Then it continues through the inner nuclear layer, the outer reticular layer, the layer of Henle's fibers and the outer nuclear layer to the membrana limitans externa. This, like the interna, is a product of the radial fibers but with this difference, that it is a true membrane with numerous perforations. From the membrane there proceed most delicate, hairlike continuations, the so-called fiber-baskets, which, like a lattice, surround a part of the inner members of the rods and cones. Pl. 81, Fig. 1

The fibrous portions of the radial glia cells differ in details in the different layers of the retina. In the inner layers, *i. e.* in the nerve fiber and ganglion cell layers, they bifurcate and form several branches which unite at the foot-plate. The chief fiberlike part Fig. 36 of the cell is in the reticular layer where it gives off numerous lateral processes in the form of delicate filaments which form the glial framework for the nervous constituents of the layer. Similar filaments are present in all the layers of the retina, but in varying degrees of development, being stoutest in the external nuclear layer. In both of the nuclear layers the fiberlike body of the supporting cell shows depressions, like niches, for the reception of the cells of these layers.

In addition to the radial fibers there are said to be present supporting elements like GLIA CELLS in the outer reticular layer where their long projections spread out parallel to its surface. True glia cells are also found at the point of entrance of the optic nerve and in small numbers in the adjacent parts of the optic fiber and ganglion cell layers.

The cerebral layer of the retina in its various parts shows the following structure: Pl. 80, Figs. 1—4 The LAYER OF NERVE FIBERS (2) consists of naked axis cylinders without medullary sheath or neurolemma. By far the greater part are axones of the cells of the ganglion cell layer; a small part are centrifugal fibers from the brain which appear to end upon various cells in the retina. The great majority of the fibers thus transmit impulses to the brain. As a result this layer continually increases in thickness from its periphery at the ora serrata to the point of entrance — or better of exit — of the optic nerve. Near the ora serrata it is so thin that it can hardly be perceived. The fibers from around the margin of the fovea centralis, *i. e.* from the macula lutea, form a special maculo-papillary bundle which runs as a compact whole from the macula to the temporal part of the optic nerve; but the other fibers of the layer run a strictly radial course toward the optic papilla.

Fig. 36 The LAYER OF GANGLION CELLS (3) or the *ganglion nervi optici* contains the largest Pl. 80, Figs. 1—3 cellular elements of the retina. They are multipolar cells with relatively short and fine dendrites but large cell bodies and relatively small nuclei. Certain cells which occur at quite regular intervals are distinguished by especially large size. Twin ganglion cells also occur. The protoplasm, like that of most of the nerve cells of the brain, shows tigroid granules, neurofibrils etc. (p. 115). The dendrites, which are profusely branched, are few in number (2—3) and always proceed from that part of the cell which is turned toward the inner reticular layer. Each cell has one axone which forms the axis cylinder of a fiber of the layer of nerve fibers, the thickness of which consequently stands in direct relation to that of the layer of ganglion cells. Proceeding inward from the periphery of the retina where the cells are scattered, they next form a single compact layer which then increases in thickness until near the macula lutea it contains several (5—8) layers of cells. The dendrites spread out in the inner reticular layer where they enter into synapses with dendrites or axones of other ganglion cells of the retina (see below).

The INNER RETICULAR or plexiform LAYER (4) contains no cellular elements at all but is a close entanglement (neuropil) of different kinds of cell processes. These are not made evident by ordinary methods of staining which show the layer as finely granular or "molecular" (p. 122). In addition to the dendrites from the layer of ganglion cells there are here present axones from the bipolar cells of the inner nuclear layer and processes from the amacrine cells.

The INNER NUCLEAR LAYER (5) is composed of very diverse kinds of cellular elements which on an average are of small size, consequently their nuclei form a compact layer. They belong to four different types of cells: 1. those of the radial fibers (p. 269), 2. bipolar cells, 3. amacrine cells, 4. horizontal cells. The BIPOLAR cells form the majority — about four-fifths — of the cells of the layer. They are small, bipolar nerve cells which as a whole are included under the name "ganglion retinae" in contrast to the ganglion nervi optici. They occupy chiefly the middle strata of the layer. Each consists of a small cell body having the form of an elongated spheroid — an ellipsoid — with relatively large nucleus and scanty protoplasm. Of its two processes the one passes centrally into the inner reticular layer where it flattens and forms an end-plate from which its terminal branches proceed; while the other extends peripherally into the outer reticular layer where it expands and resolves into a network of short branches. A distinction is made between rod bipolar and cone bipolar subtypes related respectively to rods and to cones and differing from each other in several regards.

The AMACRINE cells of the inner granular layer are larger ganglion cells than the Fig. 36
bipolar and belong to Golgi's type II, *i. e.* the axone after a short course breaks into its terminal branches, in this case within the inner reticular layer. The amacrine cells lie chiefly in the inner part of the layer and are distinguished from the bipolar cells by their greater size, while the HORIZONTAL CELLS lie at the boundary next the outer reticular layer.[1] The latter are stellate cells of various sizes concerning the significance of which but little is known.[2] Their name is derived from the essentially horizontal position of their dendrites which spread out parallel to the surface of the retina.

The outer reticular or plexiform layer (6) (internuclear layer) shows a structure similar to that of the inner reticular layer, *i. e.* it represents an entanglement of neural processes, a neuropil (p. 122). The layer is practically free from cells; only the relatively infrequent horizontal glia cells (see above) are present and certain scattered bipolar cells to which have been given the quite superfluous name of "subepithelial ganglion cells". The fibers of the rods and cones and the processes of most of the cells of the inner nuclear layer terminate in this band.

The **neuro-epithelium** of the retina appears to form three layers, Henle's layer (7), Pl. 80, Figs. 1–3
the outer nuclear layer (8) and the layer of rods and cones (10). In reality there is but Pl. 81, Fig. 1
a single element involved, the visual cell or neuro-epithelial cell of the retina. In man there Fig. 36
are two kinds of visual cells, rod cells and cone cells, of which the former are the more numerous.

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[1] A distinction is made between diffuse and stratum-forming amacrine cells. The axone of the former has its branches spread out flatly at the boundary of the inner reticular layer, while the axone of the latter sends its branches deeply into the layer and assumes a more treelike form.

[2] It is even uncertain whether they are glia cells or nerve cells although certain processes which have been taken for dendrites run to the inner ends of the rods and cones; while other processes of the same structure and considered to be axones seem to enter into relation with more distant visual cells.

The nuclei of both kinds of cells lie in the outer nuclear layer and determine its characteristic appearance; while the outer parts of the cells, under the names of rods or cones as the case may be, are incompletely separated from the parts containing the nuclei by the external limiting membrane.

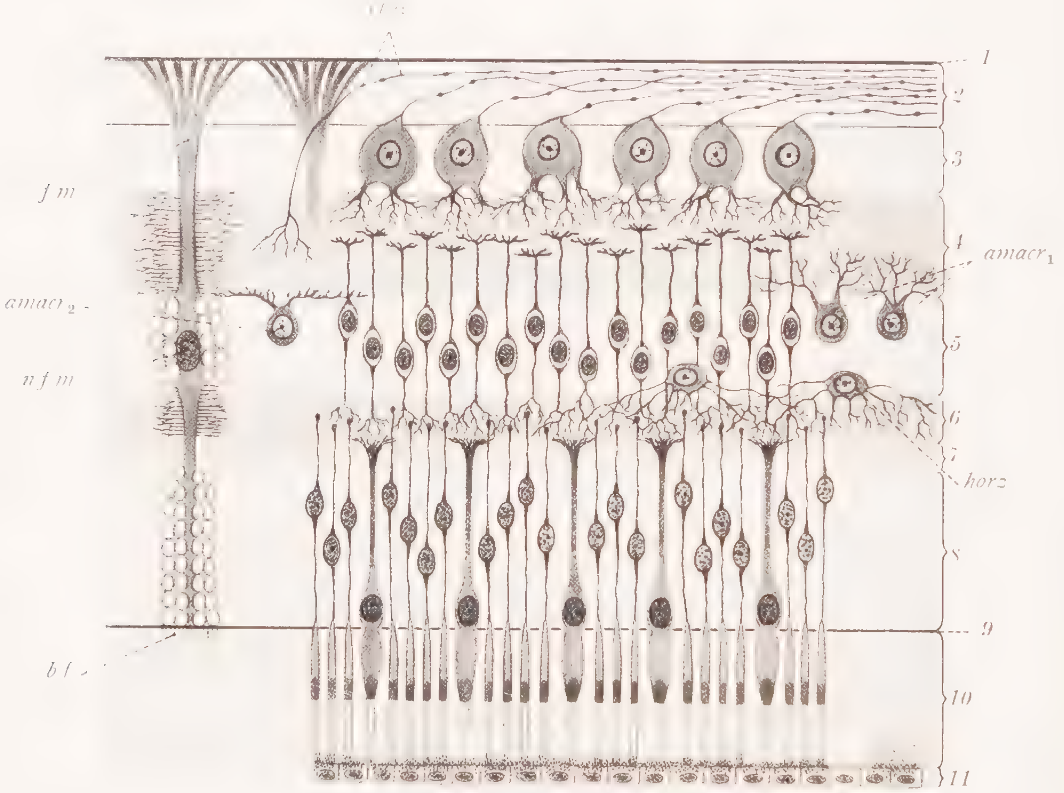

Fig. 36. **Diagram of the Structure of the Retina.**

The glial elements are shown at the left; the remaining parts of the figure represent the nervous elements. The numbers 1—11 designate the so-called layers of the retina.

1 = internal limiting membrane
2 = layer of fibers of optic nerve
3 = layer of ganglion cells
4 = inner reticular layer
5 = inner nuclear layer
6 = outer reticular layer
7 = Henle's fiber layer
8 = outer nuclear layer
9 = external limiting membrane

10 = layer of rods and cones
11 = pigmentary epithelium
amacr$_1$ = "diffuse" amacrine cells
amacr$_2$ = "stratified" amacrine cells
b f = basket fibers
cefug = centrifugal fiber
f m = fiber of Müller
horz = horizontal cells
n f m = nucleus of fiber of Müller

The ROD CELL consists in the first place of the rod itself, a cylindrical structure, 50—60 μ long and about 2 μ thick, in which a finely granular inner half or INNER SEGMENT is to be distinguished from a homogeneous outer half or OUTER SEGMENT. The base of the inner member fits into a corresponding opening in the external limiting membrane and is sur-

rounded by the fiber basket belonging to the latter (p. 270). Inner and outer seg- Fig. 36
ments of the rod are about equal in length. From the base of the rod there proceeds the rod fiber which is very slender except in the middle where there is an expansion, the ROD GRANULE, containing the nucleus. The inner end of the rod fiber lies in the outer reticular layer and expands into a small knob. Since the small, almost spherical nuclei of the rod fibers are placed at different levels in the outer granular layer, they may be either in the middle or toward one end of the fiber.

The CONE CELL consists similarly of a cone and a cone fiber. The cones, like the rods, possess inner and outer members, but the conical outer member often appears to be shorter than that of the rod, however at its middle its diameter is as great, while the inner member is much thicker and is flask-shaped. The CONE FIBER possesses an expansion, the CONE GRANULE, containing the nucleus which usually lies immediately at the base of the cone separated from it only by the internal limiting membrane. Consequently the nuclei of the cones usually lie in a single layer upon the inner surface of this membrane; but where the cones are numerous as in the macula lutea and fovea centralis there is not room for all the nuclei in one layer, consequently they form several. In this case some of the nuclei lie INWARDLY along the course of the fiber. Where the cone cell passes through the internal limiting membrane it is slightly constricted. The elliptical nucleus of the cone cell is larger than that of the rod cell. Following upon the nucleus is the cone fiber proper; although very slender it is decidedly thicker than a rod fiber. It first penetrates the outer granular layer running between the rod nuclei, then enters Henle's fiber layer and ends at the boundary of the outer reticular layer in an expanded foot. The feet of the cones standing close together at the same level may readily be observed to form a sharp line.

While the rods have always the same size in all parts of the retina both the thickness and the length of the cones vary considerably in different regions. In the middle areas of the retina the length of the cones is about 50 μ or even somewhat more, equal indeed to that of the rods. In these central areas it is noteworthy that the conical outer segment is not shorter than the thick inner segment.[1] In the region of the fovea centralis the cones become long and slender but toward the ora serrata they become short and thick, so that the most peripheral cones have short, broad, rounded, almost spherical inner segments and show only a small stump as an outer segment. The length of the outermost cones of the ora serrata is only 15 μ.

HENLE'S FIBER LAYER, (7) lying next to the outer reticular layer, is radially or obliquely Pl. 80, Fig. 2
striated and is formed of the inner ends of the rod and cone fibers, particularly of the latter. Pl. 81, Fig. 1
Only in the region of the macula lutea does it attain a considerable thickness, but there Fig. 36
it is prominent because of the predominance of the cones. The thick cone fibers produce the striation and in the region of the fovea centralis they run obliquely because of the excentric position of their nuclei (p. 275).

In the middle areas of the retina there are three or four rods to one cone, while in the peripheral parts the cones are very short, 25—30 μ, and are irregularly distributed. In the region of the macula lutea they increase in number until near the fovea centralis they predominate over the rods; on the other hand at the ora serrata there are only cones (p. 276).

The outer segments of the rods cones appear to be finely striated longitudinally due to a fine grooving of the surface. The contents of this striated envelope, if it is such, appear

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[1] The outer segment of the cones often appears shorter than that of the rods, due to the fact that it is contractile and frequently appears in preparations in its shortened condition.

under many methods of preparation to be transversely striated; *e. g.* when examined in the fluid of the vitreous humor the rods break up into transverse discs and it is assumed that they are in truth the elements of which the rods are composed. Probably the material of the outer segment is related to the medullary sheath of nerves since both are blackened by a solution of osmium tetroxide.

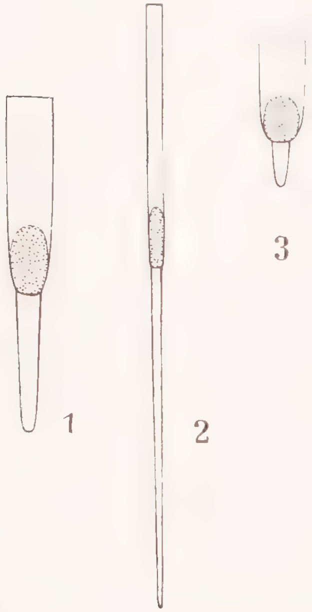

Fig. 37. **Comparative Forms and Sizes of Cones** from different regions of the retina (diagrammatic). The dotted area represents the ellipsoid. × **1,000.** Pl. 80, Figs. 1—3

1 = cone from middle area of retina
2 = long, slender cone from fovea centralis
3 = short, broad cone from margin of retina near the ora serrata.

Special methods show still finer structural features in the rods and cones, in particular fibrils in the outer segments; however their nature as neurofibrils is not generally accepted. At the border of the outer and inner segments of a cone, but within the latter segment, even ordinary methods show an ellipsoidal, longitudinally striated body, the CONE ELLIPSOID. In the rods a similar ROD ELLIPSOID is present but is less distinct. These ellipsoids are considered to be the chondriomes of the cells (p. 4). The outer segment has a higher refractive index than the inner and is doubly refractive. In the rods it is the seat of the so-called visual purple. The nuclei of the rod cells of many mammals, *e. g.* the cat, show the chromatin in transverse bands, but in man there is only a trace of this arrangement.

In the sense of the neurone theory (p. 111) three neurones are to be distinguished in the retina: peripherally the visual cell, in the middle the bipolar cell, and centrally the cell of the ganglion nervi optici. In addition connections are established between different parts of the retina through the horizontal and amacrine cells.

The rods and cones receive the sensory stimulus since they are the constituents of the neuro-epithelium adapted to this function. They pass it on to the middle neurones, the bipolar cells. One rod bipolar receives the stimulus from several rod cells, but a cone bipolar is connected with only one cone cell. This explains why the number of bipolar cells and the thickness of the inner nuclear layer increases with the number of cones, as in the macular region; and why, in those areas of the retina where the number of the rods is greater than that of the cones, the outer nuclear layer is considerably thicker than the inner. That the inner nuclear layer may become even thicker than the outer, as in the inner part of the macular region, depends upon the fact that at the fovea centralis there are only a few scattered bipolar cells and at the bottom of the fovea none at all. Consequently the feet of the foveal cones must run to the bipolar cells lying at the border of the fovea; hence the oblique courses of the cone fibers in the foveal region. As a result the inner nuclear layer of the macula lutea contains not only the nuclei of the bipolar cells of its own area but also those of the fovea centralis.

The transmission of the stimulus from the neurones of the inner nuclear layer (bipolar cells) to those of the layer of ganglion cells (ganglion nervi optici) is quite similar. In the peripheral region of the retina the ganglion n. optici is composed of a single layer of cells; but as the cone bipolar cells increase in number the ganglion cells also become more numerous, until in the foveal region they are arranged in several layers. It must also be assumed that since a special cone bipolar cell belongs to each cone visual cell, the latter can transmit its stimulus to only a single cell of the ganglion n. optici; while the strikingly small number of cells of the latter layer in the areas in which the rods predominate, is explained by the fact that a single cell of the ganglion n. optici receives a stimulus from several rod bipolar cells. Or, in other words, the stimulus which a nerve fiber of the optic nerve carries to the brain has been received either from a single cone visual cell by way of ONE cone bipolar cell, or it has been taken over from quite a number of rod visual cells by the intervention of several rod bipolar cells. Or, to express it differently, the majority of the fibers of the optic nerve transmit stimuli which come from the cones, notwithstanding the fact that the latter are in the minority; while the minority of the fibers of the optic nerve transmit stimuli from the rods although the latter predominate. Or, again — from the region of the macula there come relatively many more fibers of the optic nerve than from the peripheral areas of the retina.

The structure of the pars optica retinae is not everywhere the same, in particular it grows gradually, but decidedly, thinner toward the periphery and at the ora serrata a reduction of the inner layers is noticeable. Here the coat is only 0.05—0.1 mm. thick as against 0.3 mm. at the posterior part of the eye. Three areas of the retina differ decidedly from the retinal structure as described above: 1. the macula lutea and fovea centralis, 2. the ora serrata, 3. the optic papilla.

The *macula lutea* is a poorly defined area of the retina, its boundaries are vague and the extent of the yellow pigment is highly variable. The structure of its central depression, the **fovea centralis,** will be first considered. This area is characterized by an extreme reduction of all the cerebral layers of the retina. Only the neuro-epithelial layer is well developed, and of it chiefly the cones. The thinnest place is the bottom of the pit, the *fundus foveae*, where the entire thickness of the retina amounts only to 0.15 mm., more than half of which is due to the extraordinarily long cones which give to the retina even here a thickness greater than at the ora serrata. The FOVEAL CONES do not stand so close together over the bottom of the pit as they do toward its margins. Their length is 80—90 μ while elsewhere cones average only 50 μ, thus they are considerably longer than the rods (60 μ); at the same time they are extremely slender (1.5 μ), more so than the rods. In spite of this the form of the cones is preserved *i. e.* the inner segment is almost cylindrical and is thicker than the outer segment which tapers like a cone toward its end. Because of the great length of the foveal cones the external limiting membrane at the bottom of the fovea centralis is arched toward the interior of the eye, forming the so-called "FOVEA EXTERNA".[1] Altogether the remaining layers of the retina in the region of the fundus foveae are diminished to less than half their usual thickness and are very strongly reduced without failing completely. The layer of nerve fibers is but slightly developed and at the fundus foveae is entirely lacking. The layer of ganglion cells is still quite well developed up to the margin of the fovea centralis, but in the fovea it is reduced to a few scattered cells and is entirely lacking at the bottom of the pit. The same is true of the inner nuclear layer. In place of the two reticular layers there appears a narrow zone of plexiform character which is the only remnant of the cerebral layers of the retina that a ray of light needs to penetrate at the fundus foveae. Henle's fiber layer and the outer nuclear layer are somewhat more strongly developed; representing the latter one or two rows of scattered nuclei may be observed lying at the bottom of the fovea. Pl. 80, Fig. 3 Fig. 37

Toward the margins of the fovea centralis the cones diminish markedly in length while their thickness increases until doubled. The "fovea externa" disappears. Finally in the macula lutea isolated rods appear but the cones still predominate markedly. The remaining layers of the retina increase in thickness toward the margins of the fovea, so Pl. 80, Figs. 2, 3 that in the macula lutea the coat attains a considerable thickness (almost 0.3 mm.) and the cerebral layers are no less strongly developed than is the neuro-epithelium. The layer of nerve fibers is thick, there are 5—9 layers of ganglion cells and an equally thick inner nuclear layer, which throughout the whole macular region exceeds the outer nuclear layer in thickness.[1] That its "fibers" in part show a necessarily oblique course has already been explained (p. 274). Henle's fiber layer is very distinct.

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[1] Considering the long foveal cones removed so as to expose the external limiting membrane, the latter appears as a shallow but distinct depression on the outer surface of the retina.

Pl. 77, Fig. 1
Pl. 80, Fig. 5
The **ora serrata** marks the boundary between the pars optica and the pars ciliaris retinae. In its neighborhood, corresponding to the diminution in thickness of the coat, there is a gradual reduction of the nervous constituents of the retina while the supporting elements remain as ever. First of all the layer of nerve fibers diminishes in thickness and the ganglion cells in number so that only a single cell will occur now and then at great intervals; while the outer and inner nuclear layers come together and the outer reticular layer disappears. Just behind the ora serrata the inner reticular layer practically ceases and in place of the two nuclear layers there are only scattered nuclei belonging for the most part to the fibers of Müller. The pars optica retinae shows here its minimum thickness — about 50 μ.[2] Cones are present almost to the ora serrata while the rods cease a little further behind it. The last cones are extraordinarily short, 15 μ and less as against 50—60 μ in the posterior part of the eye, and have only very short external segments, like stumps, which rest on broad and rounded internal segments. At the ora serrata itself all the nervous constituents of the coat disappear and the supporting elements pass quite sharply into the epithelium of the pars ciliaris retinae.

Concerning the optic papilla see under Optic Nerve.

b. ***Pars caeca retinae***

The pars caeca retinae is subdivided into the pars ciliaris and the pars iridica.

Pl. 79, Fig. 3
Pl. 80, Fig. 5
Pl. 81, Figs. 4, 5
The *pars ciliaris retinae* begins at the ora serrata and extends to the outer margin of the iris. It consists of a single layer of epithelial cells varying from high-cubical to columnar in form and from 20—25 μ in actual height, those near the ora serrata being the longer. They rest on the pigmentary epithelium (p. 268) to which they are firmly connected and bear on their surface a structureless cuticle which is a direct continuation of the internal limiting membrane. Fibers of the zonula ciliaris (p. 279) arise from their inner surface interrupting the cuticle at their points of origin.[3]

The *pars iridica retinae* covers the posterior surface of the iris up to the pupillary margin where it becomes continuous with the pigmentary epithelium. It forms with the latter the pigmentary layer of the iris, and in contrast to the pars ciliaris it bears pigment. The posterior surface of the cells is covered by the same fine structureless cuticle as occurs on the pars ciliaris. The posterior surface of the iris is thus covered by a doubled and pigmented epithelium (p. 268).

The cells of the epithelium are columnar and although often quite long they bear at their bases relatively small nuclei. The cell body is completely filled with particles of fuscin pigment so that their nuclei and boundaries are visible only after depigmentation. The epithelium forms circular folds which become higher as the iris contracts and the pupil widens; when the pupil is narrow they become more or less flattened.[1] The pronouncedly dark color of the posterior surface of the iris is primarily due to the intense pigmentation and depth of cells of its pigmentary epithelium. Moreover the thickness of the epithelium increases from the root of the iris to the pupillary margin where the edge of the optic cup turns forward into the pupillary opening proper and thus lines the extremely short pupillary canal.[2]

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[1] The macula can be readily distinguished from the peripheral retina by the comparative thickness of the nuclear layers. Outside the macula the thickest layer is the outer nuclear, then comes the inner nuclear and last the layer of ganglion cells. In the macula this order is just reversed.

[2] Just behind the ora serrata vacuoles often form in the middle layer of the retina. Occasionally they are of considerable size, and greatly disturb the structural picture of the coat.

[3] For the relation of the cells of the pars ciliaris to the zonula ciliaris and to the vitreous body see page 279.

The **blood vessels** of the retina occur only in its visual part. They belong to the system of central vessels (vasa centralia retinae) and do not stand in close relationship to the remaining vessels of the eye.[3] The *arteria centralis retinae* enters the retina with the optic nerve at the so-called optic papilla, from which point its branches spread out in approximately radial directions.[3] The larger branches lie in the nerve fiber and ganglion cell layers of the retina and form a fine capillary network which extends through all the cerebral layers as far as the outer reticular layer; peripherally it does not quite reach the ora serrata. The bottom of the fovea centralis is entirely devoid of vessels. The *vena centralis retinae* has the same distribution as the artery. The arteries of the retina have an unusually weak coat of circular muscle and the veins have practically no muscle at all. The entire eyeball, including the retina, is devoid of lymphatic vessels.

c. *Optic Nerve and Optic Papilla*

The optic nerve, *nervus opticus*, consists of the nerve trunk proper and its sheaths. The former is not a true nerve but a cerebral fiber-tract and on this account its structure Pl. 82
is entirely different from that of ordinary peripheral nerves. The sheaths are the same as Pl. 77, Fig. 1
those of the brain (p. 174), dura mater, arachnoidea and pia mater (dural, arachnoideal and pial sheaths); and show a structure similar to theirs. At the entrance of the optic nerve into the eyeball the dural sheath passes without demarcation into the sclera and the arachnoidal and pial sheaths blend with the tissues of the chorioidea. The pial sheath closely invests the optic nerve and sends into its interior numbers of fibrous connective-tissue strands which, with the addition of neuroglia, form branching septa. These septa carry the vessels (p. 278) and form the boundaries of several hundred (800—1000) rounded or polygonal bundles made up of varying numbers of nerve fibers. The individual bundles are not everywhere completely surrounded, nor does the pia mater enter their interior. The bundles consist of the long-rayed type of neuroglia and of naked axis cylinders and fine medullated nerve fibers without neurilemma; thus they show the structure of the white substance of the brain, not that of peripheral nerves. The neuroglia is especially well developed on the surface of the bundles and of the nerve as a whole. In the latter situation it forms the peripheral neuroglial mantle which is so closely united with the connective tissue of the pia mater that the two can be sharply distinguished only with the help of special methods of staining.

The fibers of the optic nerve arise within the retina and are the direct continuations of the fibers which form the innermost nervous layer of the coat. This statement disregards the centrifugal fibers — see Fig. 36 — the existence of which is not definitely proven. Fibers coming from all parts of the retina converge radially to the point of exit of the optic nerve. However the fibers from the region of the macula lutea form a relatively important bundle — the MACULO-PAPILLARY bundle — which passes directly to the neighboring "papilla". (For the remarkably large number of fibers in this bundle see page 275.)

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[1] These folds are like the "gathers" of dressmaking, the epithelium being the material which is "gathered".

[2] Strictly considered the pupil is not a perforation but a short canal.

[3] See pages 267 and 278, also Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III.

The area into which all the axones of the cells of the ganglion nervi optici converge has the form of an almost exactly circular disc that is very slightly raised above the level of the surrounding region of the retina. The diameter of this disc is 1.7 mm. and its thickness 0.4 mm. It looks white[1] and is slightly excavated in the middle. It has long borne the somewhat undeserved name of **papilla nervi optici.**[2] The fibers of the retina which have concentrated at the papilla now form separate bundles and penetrate the sclera (lamina cribrosa sclerae — see above) after which they acquire very thin medullary sheaths.[3] Not until this point is reached is there truly formed an optic nerve with the structure described above.

About 1½ cm. from the point where the optic nerve emerges from the eyeball (long erroneously termed the "point of entrance of the optic nerve") the vasa centralia retinae enter into the nerve trunk and with it reach the retina. A sheath of pia mater accompanies the vessels between the bundles composing the optic nerve to reach a central position in the latter.

The BLOOD VESSELS of the optic nerve are the vasa centralia which before reaching their distribution in the retina send branches into the trunk of the nerve and there enter into a few anastomoses with the neighboring ciliary vessels. Lymphatic vessels are lacking in the optic nerve but LYMPH SPACES are present comparable to the subdural and subarachnoidal sinuses of the meninges.

4. The Lens

Pl. 77, Fig. 1 The lens, *lens crystallina*, is entirely an epithelial structure, peculiar to the eye, per-
Pl. 79, Figs. 2, 5 fectly transparent and devoid of blood vessels. It consists of three parts, capsule, epithelium
Pl. 81, Fig. 2 and substance of the lens.

The capsule of the lens, *capsula lentis*, is a homogeneous, structureless membrane surrounding the entire lens.[3] On the anterior surface of the lens near the anterior pole its thickness is 15—20 μ, toward the equator this diminishes to 10—12 μ. Over most of the posterior surface the thickness is reduced to 4 μ or less, but near the equator a sudden increase occurs like a band surrounding the lens.

The epithelium of the lens lies inside the capsule and is strictly limited to one layer of cells which covers only the anterior surface of the lens. The cells are of low-cubical form near the anterior pole but increase in height toward the equator. The epithelium is wanting on the posterior surface of the lens because at the equator it passes over into the lens fibers. In the equatorial region the epithelial cells are about 10 μ high, cubical or low-columnar and no longer stand perpendicular to the surface of the lens but incline so that the angle which they form with the surface of the lens becomes less and less. At the same time the cells gradually enlarge into fibers, the lens fibers, which run a meridional course and become ever longer and longer.

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[1] As to the white color of the optic papilla and the gross anatomical relations see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III.

[2] At least this is the rule. However a few medullated bundles are still found on the optic papilla. The sclera is particularly rich in elastic fibers at the lamina cribrosa; while the chorioid coat is merely perforated and does not share in forming the latter structure. Naturally the sheaths of the optic nerve, including the pial sheath, cease at the inner surface of the lamina cribrosa.

[3] It is negatively doubly-refractive.

The substance of the lens, *substantia lentis*, consists of the lens fibers, *fibrae lentis*, long, thread- or band-like structures of flattened, hexagonal-prismatic form with thickened, clublike ends. They are 2—4 μ in thickness and 5—10 μ in breadth. Three kinds of fibers can be distinguished in the fully developed lens, chief, transitional and central fibers. The chief fibers form the main mass of the lens, the cortical layer, *substantia corticalis lentis*. They have smooth borders and near the equator where they pass into the epithelium of the lens, show an elongated nucleus. Originally all the fibers possess nuclei but those of the transitional fibers mostly degenerate, as do all those of the central fibers. The transitional and central fibers have wavy or notched borders and form the firm nucleus of the lens, *nucleus lentis*.[1] The fibers of the lens are fastened together by a small quantity of cement substance. Particularly at the equator the lens fibers, lying with their broader surfaces parallel to the surface of the lens, form very distinct lines in which, however, divisions often occur.

Pl. 81, Fig. 2

The lens contains neither vessels nor nerves.

5. The Vitreous Humor and the Zonule of Zinn

The **VITREOUS HUMOR**, *corpus vitreum*, and the zonule of Zinn, *zonula ciliaris*, by development belong together. Both are ectodermal retinal supporting tissues produced by the supporting elements of the retina with which they stand in intimate connection. The vitreous body is an exceedingly watery mass of tissue (almost 99% water!) which consists of very fine glial fibers interlacing to form a network the meshes of which are filled with fluid. The fibers become more numerous toward the surface where they form a kind of limiting layer, the so-called hyaloid membrane. In the anterior parts of even the adult retina the network of the limiting layer may still be seen connected with the fibers of Müller and near the ora serrata the connection with the columnar cells of the pars ciliaris retinae is even more distinct. In addition to the network of fibers there occur in the vitreous humor wandering cells and, especially in young individuals, a few isolated, fixed cells of stellate form.[2]

Pl. 81, Fig. 6

The **ZONULA CILIARIS** consists entirely of quite stout, firm and perfectly structureless fibrils which take their origin from the cells of the pars ciliaris retinae in the region of the orbiculus ciliaris. They are connected with the cells of the pars ciliaris retinae just as those of the vitreous humor are with the fibers of Müller in the retina; but with this difference that they arise more anteriorly from the cells of the orbiculus ciliaris. The greater part of the fibers arise immediately in front of the ora serrata but in their course forward receive constant reinforcements of fibers from cells which lie still further forward. By the repeated fusions of thin fibers the fibers of the zonula become thicker and thicker the nearer they approach the lens. They run through the depressions between the ciliary processes to the equatorial region of the lens where they are inserted in three rows, one on the anterior surface, a second at the equator itself and the third on the posterior surface. The latter group

Pl. 77, Figs. 1, 2
Pl. 79, Figs. 2, 4

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[1] Concerning the course of the fibers, the lens-stars etc. see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III.

[2] Recent results which have again appeared in support of the presence of collagenous tissue in the vitreous humor are based upon error. The superficial part of the network simulates a lamellar arrangement.

contains only very fine fibers which spring from the sides of the ciliary processes. The anterior and posterior fibers of the zonula are clearly arranged in bundles which produce the indentations at the equator of the lens. The spaces bounded by the fiber bundles of the zonule and the equator of the lens are termed the *spatia zonularia* or canal of Petit. The fibers of the zonule differ greatly in thickness, very fine fibers occur and also very thick ones, up to 35 μ. Such thick fibers as this are formed by fusion with the reinforcing fibers and occur only in the posterior region of the zonule.

The adult vitreous humor is entirely free from vessels. In the embryonic state it contained the *vasa hyaloidea*, continuations of the central vessels of the retina, which run to the posterior surface of the lens in a canal that usually persists as the hyaloid canal. The vitreous humor contains no nerves.

Accessory Organs of the Eyeball

1. The Eyelids and the Conjunctiva

The **eyelids,** *palpebrae*, are folds of the skin, which on their outer surface show the ordinary characteristics of the skin, while on their inner surface they are covered by the conjunctival mucous membrane. In its interior each lid contains, in addition to muscle, the so-called cartilage of the lid, the tarsus, a strong, fibrous plate almost as hard as cartilage.

In the eyelid the following layers are distinguished from in front backwards: 1. The Pl. 83, Figs. 1—3 skin with lanugo hairs, sebaceous glands, etc. 2. subcutaneous tissue, 3. the palpebral portion of the musculus orbicularis oculi, 4. loose connective tissue with the chief vessels of the lid, 5. the tarsus with the tarsal glands, 6. the tunica conjunctiva palpebrarum.

The skin of the eyelid is extremely fine and thin and is devoid of fat, but shows no essential peculiarities such as might be expected; for the lanugo hairs are rather numerous and both sebaceous and sweat glands are present. The corium not infrequently shows scattered, branched connective-tissue cells containing small quantities of pigment. At the border of the eyelid the stratum corneum ceases, the papillae become higher and the skin gradually passes into the conjunctiva. At the anterior edge of the border of the eyelid are found the eyelashes, *cilia*, stout body hairs arranged in two or three rows and distinguished from similar stout hairs elsewhere on the body by being shed with great frequency and regularity; as a result club hairs are often found among them.[1] The eyelashes possess Pl. 90, Figs. 4, 5 sebaceous glands, so-called glands of Zeiss, but no musculi arrectores. Although short they are relatively strong and are implanted very obliquely.

The tubular GLANDS OF MOLL, *glandulae ciliares*, are found near the eyelashes; by Pl. 83, Fig. 3 their structure these are sweat glands and must be assigned to the apocrine type of larger sweat glands such as those of the axilla. Their coiled portion is neither compact nor well developed. Some bundles of the *m. palpebralis* lying under the thin skin of the lid are inserted between the eyelashes and the inner edge of the lid and are described as the *m. tarsalis* (inferior-ciliaris Riolani). These bundles of striated muscle also surround the openings of the tarsal glands to a variable extent. The main mass of the m. palpebralis lies in the middle of the lid separated from the skin by a small quantity of loose, subcutaneous connective tissue and from the tarsus by the pretarsal connective tissue. The latter, in addition to adipose tissue which gradually appears toward the base of the lid, also contains the larger NERVES and VESSELS and near the roots of the eyelashes the arterial tarsal arches.

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[1] The life of an eyelash is estimated at 40—50 days, a contrast to that of the hairs of the head (p. 304).

The CARTILAGE OF THE LID, *tarsus*, histologically is not a cartilage but is formed of dense fibrous connective tissue whose bundles are so firmly interwoven that the structure attains the consistency of cartilage. Throughout its entire length it is penetrated by the Meibomian glands, *glandulae tarsales*, a variety of sebaceous gland supplying the *sebum palpebrale* and in minute structure exactly similar to the sebaceous glands of hairs. They possess a long median duct which is surrounded on all sides by alveoli. The short, but wide, excretory duct proper no longer bears alveoli but is lined by stratified pavement epithelium and discharges immediately in front of the inner edge of the eyelid. The tarsus does not extend to the base of the lid.[1] In the tarsus lie also parts of a few other glands (see below) and around the terminations of the Meibomian ducts there are the above mentioned striated fibers of the m. tarsalis (ciliaris Riolani).

Pl. 83, Fig. 1

The posterior surface of the tarsus is covered by the conjunctiva of the eyelid, *tunica conjunctiva palpebrarum*, which has grown firmly to the tarsus. Its tunica propria consists of connective tissue which contains elastic fibers and in most places is quite compact. It contains many lymph and plasma cells which in the region of the fornix conjunctivae may form solitary follicles *(noduli lymphatici conjunctivales)*. There are no papillae in the mucous membrane of the palpebral conjunctiva; it has a stratified columnar epithelium of several rows of rounded cells and a superficial layer of columnar cells but there are local differences even within the range of the eyelid. Toward the margin of the lid stratified squamous epithelium occurs and near the fornix of the conjunctiva the epithelium becomes more markedly stratified. Goblet cells are abundant. Small glands with the structure of lacrimal glands, *glandulae mucosae conjunctivales* (accessory lacrimal glands, glands of Krause or of Wolfring) are present near that margin of the tarsus which is turned toward the base of the eyelid. They are largely and often completely embedded within the substance of the tarsus. In this region and toward the fornix of the conjunctiva the epithelium often shows numerous marked papillary outgrowths consisting largely of lymphatic tissue.

Pl. 83, Fig. 1

The tendon of the *m. levator palpebrae superioris*[2] joins the upper free margin of the tarsus of the upper eyelid and shows a subdivision into two parts. The anterior part is a purely connective-tissue radiation that blends with the pre-tarsal connective tissue between the palpebral muscle and the tarsus. The posterior part is so intimately combined with the superior tarsal muscle which consists of non-striated fibers that the striated muscle of the levator palpebrae and the fibers of smooth muscle are scarcely to be separated.

The **conjunctiva,** *tunica conjunctiva*, is subdivided into that of the eyelids, *tunica conjunctiva palpebrarum*, and that of the eyeball, *tunica conjunctiva bulbi*. The two subdivisions meet at the *fornix conjunctivae (conjunctiva mobilis)*. The structure of the palpebral conjunctiva has been already described. The bulbar conjunctiva differs from the palpebral in having low papillae and a stratified squamous epithelium which, at the margin of the cornea, is continuous with the corneal epithelium (p. 261).

Pl. 77, Fig. 1
Pl. 83, Fig. 1

A third eyelid, the *plica semilunaris conjunctivae*, is very rudimentary in man although greatly developed in many mammals. It is covered by squamous epithelium but also contains goblet cells. The latter are not altogether lacking in the remaining parts of the conjunctival epithelium. This is true even for the thick epithelium of the caruncula lacrimalis which has coiled sweat glands, sebaceous glands, and small lanugo hairs, as well as scattered fibers of striated muscle. Its corium is rich in lymphoid cells.

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[1] See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III.

[2] See Sobotta-McMurrich, Atlas of Human Anatomy, Vols. I and III.

The BLOOD VESSELS of the upper eyelids form anastomatic arches; one, the *arcus tarseus inferior*, lies near the border of the lid, and is usually the stouter, the other, the *arcus tarseus superior*, lies at the base of the lid.[1] Capillaries arise from both arches and run to the tarsus, to the musculature and to the skin of the eyelids. In contrast to the eyeball the eyelids possess LYMPHATIC VESSELS in the form of conjunctival, pretarsal and subcutaneous capillary networks which are connected with one another, even through the tarsus itself.

The eyelids are also rich in NERVES which form plexuses in the conjunctiva and in the skin; there is also a pretarsal nerve plexus. Beside free terminations in the epithelium there are present sub-epithelial end bulbs (p. 181) which extend as far as the margin of the cornea. Typical tactile corpuscles of Meissner are also present.

2. The Lacrimal Apparatus

The lacrimal apparatus, *apparatus lacrimalis*, consists of the lacrimal glands, the lacrimal ducts, the lacrimal sac and the naso-lacrimal duct.

Pl. 83, Figs. 4, 5 The lacrimal glands, *glandulae lacrimales*, (superior and inferior) are compound tubulo-alveolar glands with several excretory ducts. The secreting parts have relatively wide lumina and are lined with epithelium which is cylindrical when full of secretion[2] but which is cubical when exhausted. In the glandular epithelium granules of different forms may be observed, among which fat droplets are constantly present. Intercellular secretion canaliculi are also to be found. External to the glandular epithelium there follows a much interrupted layer of flat, contractile cells with fibrillar striation (basket or myo-epithelial cells) followed in turn by an apparently structureless membrane propria. The secreting parts of the lacrimal glands consequently resemble those of a serous salivary gland.

The interstitial tissue of the lacrimal glands is remarkably well developed and contains an abundance of adipose tissue and numerous lymph cells. Consequently the glands, particularly the inferior lacrimal gland, give the impression macroscopically of being far from compact.

The excretory ducts of medium and large size have a columnar epithelium of two rows of cells. Connection with the secreting part is made by a rather narrower portion with simple low cubical epithelium somewhat, but not altogether, like an intermediary duct of the salivary glands.

The BLOOD VESSELS resemble those of the salivary glands. They form close capillary networks around the secreting parts. The NERVES are said not merely to penetrate the membrane propria and terminate between the cells but even to have intracellular terminations.

The LACRIMAL DUCTS, *ductus lacrimales*, have a stratified pavement epithelium, a tunica propria rich in elastic fibers and a few striated muscle fibers from the pars lacrimalis m. orbicularis oculi.

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[1] Similar but less perfect arches lie in the lower eyelid. — Trans. note.

[2] Many authors distinguish two types of gland cells; high cells, whose height varies with the stage of secretion, and low cells which appear much darker and contain masses of secretion filling the entire part of the cell next to the lumen, nucleus and protoplasm being crowded together into a small space at the base of the cell.

The LACRIMAL SAC, *saccus lacrimalis*, and the NASO-LACRIMAL DUCT, *ductus nasolacrimalis*, have a columnar epithelium of two rows of cells; towards the nasal cavity cilia appear. In the lacrimal sac there are also present small tubular glands. The tunica propria is very rich in lymph cells and contains wide veins, thus resembling the mucous coat of the nasal cavity.

XI. The Organ of Hearing

1. The Internal Ear

The internal ear is represented by the so-called membranous labyrinth.[1] Of the parts of the membranous labyrinth the sacculus, utriculus and semicircular canals have approximately the same relatively simple structure, while the membranous cochlea presents special and decidedly more complicated relations, as for instance, the manner in which it is fixed within the bony labyrinth. Within the sacculus, utriculus and ampullae of the semicircular canals the terminations of the vestibular nerve lie in a modified epithelium (neuro-epithelium); while the region of the still more highly modified neuro-epithelium of the spiral organ of the cochlea contains the terminations of the cochlear nerve. The so-called "internal ear" represents the combined sense organ of the senses of equilibrium and hearing.

The cavities of the various parts of the membranous labyrinth are filled with endolymph.[1]

a. Sacculus, *sacculus*, Utriculus, *utriculus*, and Semicircular Canals, *ductus semicirculares*

With the exception of the areas of the maculae or cristae acusticae (see below) the wall of these canals and chambers is extremely thin (about 5 μ) and consists of 1. a layer of simple squamous epithelium, 2. a structureless basement membrane which in the semicircular canals often forms little knobs projecting into the lumen, 3. a tunica propria which consists of nucleated lamellae of connective tissue, 4. a layer of loose connective tissue which in part is directly attached to the periosteal lining of the inner surface of the bony cavities and in part is joined to it by fine threads of connective tissue, (ligamenta ductuum, ligamenta sacculorum), which cross the perilymphatic space. The semicircular canals are markedly eccentric within the bony canals. The wall of the convex border of each rests against the inner wall of its bony canal, while the wall of the opposite border is separated by considerable perilymph from the corresponding bony wall. Along the line where the membranous canal is attached to the bony wall the epithelium for a short distance is higher, almost cubical. Pl. 84 Pl. 84, Fig. 3

The *maculae* of the sacculus and of the utriculus and the *cristae* of the semicircular canals show a certain similarity to one another in structure; but their structure differs essentially from that described above for the rest of the wall. In the first place the epithelium, basement membrane and tunica propria attain a considerably greater thickness, and secondly within this higher epithelium there is a differentiation of cells which is connected with the nerve terminations present there.

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[1] See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III.

As regards the structure of the **maculae acusticae**[1] the epithelium, which in general Pl. 84, Fig. 2 is flat, changes to columnar as it surrounds the macular region and then passes into the true NEURO-EPITHELIUM; but its cells remain in a single layer. The neuro-epithelium is about 40 μ thick and contains two kinds of cells: 1. hair cells, 2. SUPPORTING OR THREAD CELLS. The latter are long cells reaching through the whole thickness of the epithelium; however the nucleus and most of the cell body lie in its deeper part. While the middle portions of the cells are thin and threadlike the upper, free end of each cell is expanded; the lower end is also expanded and in addition contains the nucleus. In contrast to the hair cells, which are the true sensory cells, the free ends of the supporting cells bear no hairs but form a kind of end-plate with a cuticular marginal ring. From end-plate and ring supporting fibrils proceed toward the base of the cell. The nuclei of the supporting cells are small and spherical without peculiarities.

The hair or sensory cells of the maculae commonly alternate with the supporting cells so that each hair cell is flanked on both sides by a supporting cell. They probably extend through the whole thickness of the epithelium, but the part of the cell containing the nucleus lies near the surface of the epithelium, a point of contrast to the supporting cells. The nucleus is larger than that of the supporting cells, but is pale and poor in chromatin; usually it is a true sphere. Thus the sensory cells are thickest in the upper part of the epithelium just where the neighboring supporting cells are thinnest, seeming to be compressed by the thick part of the hair cells.[2] Toward the basement membrane the hair cells become thinner; in form they resemble a rounded flask whose neck is toward the basement membrane. On their upper surface they bear a kind of cuticular end-plate from which proceed the sensory hairs proper. Each cell has a tuft of very fine hairs which are firmly cemented together so that the whole tuft runs to a point above. The length of the hairs is about 40—50 μ, or one and a half times that of the cells themselves.

The points of these tufts of hairs project into a peculiar gelatinous mass that covers Pl. 84, Fig. 2 the whole epithelium. Frequently the hairs bend at a right angle and run horizontally in the jelly. On its surface lie the otoliths, or better statoliths, and form as it were an OTOLITHIC MEMBRANE. The otoliths are small crystalline particles of calcium carbonate, which in man have dimensions of but 3—5 μ and appear to be arranged in several (3—6) layers. Their form is that of a short, irregular ellipsoid or rounded prism; hence they are also known as otoconia or statoconia. They dissolve in even very dilute acids; yet apparently the calcium is combined with an organic matrix since after it is removed by solution in acids a remnant of the statolith still remains.

The macula of the sacculus and the macula of the utriculus show absolutely the same histological structure. Macroscopically they differ, for the macula utriculi has the form of an irregularly curved spoon, while the macula sacculi appears flat and has an elliptical form. The greatest length of both maculae is about 3 mm. but the long axis of the one stands at right angles to that of the other; and on the whole the macula utriculi is somewhat the larger.

The three **cristae** ACUSTICAE or better, AMPULLARES, of the semicircular canals are Pl. 84, Fig. 4 identical in structure and in general resemble the maculae, although differing in details. At the summit of the epithelial covering of the ridge which projects into the endolymphatic space of the ampulla there occurs, as in the maculae, a differentiation into supporting cells and hair or sensory cells. The slope of the ridge, the so-called planum semilunatum, is covered by a simple columnar epithelium. The parts of the supporting cells which contain the nuclei lie near the base of the epithelium, while the corresponding parts of the sensory cells are nearer its free surface. The ends of the supporting cells are broad where they rest on the basement membrane. Their nuclei are somewhat larger than those of the supporting cells of the maculae, and more ellipsoidal; and their free ends are just like those of the macular cells, although the supporting fibrils within the cells do not extend so deeply into the basal part. The sensory cells show rather more divergence from those of the maculae. In the first place the hairs are much longer, more than 40 μ, and consequently at least twice as long as the cells. They are stuck together in a cement and form an elongated tuft which ends in an extremely fine point.

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[1] It is recognized that the term "acusticae" is incorrectly applied.

[2] The cells contain a large proportion of water absorbed from the endolymph, and on this account shrink to an unusual degree during fixation.

Corresponding to the flat, gelatinous, otolithic membrane which rests on the surface of the macula, there is at the summit of the crista a jelly-like layer covering its neuro-epithelium, the so-called CUPULA (terminalis). The latter however is high and conical, projecting far into the cavity of the ampulla, and is of extraordinarily soft consistency. The sensory hairs of the crista project into the base of the cupula which contains canals for their reception. The height of the cupula is several times that of the neuro-epithelium.

With the exception of the ductus cochlearis described below, the remaining parts of the membranous labyrinth show no peculiarities of structure.

The maculae and cristae are supplied by the branches of the VESTIBULAR NERVE, that is to say by the distal fibers (dendrites) of the bipolar cells of the vestibular ganglion. These fibers are medullated, many of them are thin (about 2 μ); but a few are rather Pl. 84, Fig. 4 thicker. All the fibers lose their medullary sheaths upon reaching the epithelium, or very shortly afterward as they pierce the basement membrane and enter the epithelial layer itself. The terminal branchings show different peculiarities according as to whether the fibers are thick or thin. The latter run chiefly to the marginal zone of the neuro-epithelium and form, under the hair cells, branching terminations which are rather of the type of simple nerve endings. On the contrary the thick fibers, together with some of the thin, form plexuses which surround the bodies of the hair cells like basketwork and thus enter into more intimate union with the cells than do the thin fibers.

b. The Cochlea, *cochlea*[1]

The membranous cochlea, *ductus cochlearis*, is a spiral canal of 2½ turns, triangular Pl. 85 in cross-section[2] and lined by an epithelium which in places is greatly modified. Laterally the wall of the canal blends with the periosteal lining of the interior of the bony cochlea so that it is not possible to distinguish everywhere a separate connective-tissue wall for the duct itself. Its boundary toward the scala vestibuli is formed by the thin *membrana vestibularis* (Reissner's membrane); while its lower wall is represented by the *lamina basilaris (lamina spiralis membranacea)* and the free border of the *lamina spiralis ossea.*

The epithelium of the tympanal wall (lamina basilaris) of the cochlear duct is modified to form a neuro-epithelium of very complicated structure, the so-called *organon spirale*

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[1] Concerning the bony cochlea etc. see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III.

[2] The shape of the duct changes from its vestibular blind end to its termination at the cupola. At first its cross-section is a flattened triangle, then the triangle becomes almost equilateral; toward the end the figure is that of an elongated oval.

Pl 85, Figs. 2, 3

or organ of Corti, which is the true organ of hearing. On the vestibular and lateral walls the epithelium is of much simpler nature. The vestibular membrane is very thin and tightly stretched and separates the ductus cochlearis from the scala vestibuli. It consists of a thin connective-tissue membrane with flat nuclei, which is continuous with the periosteum of the scala vestibuli, and of the epithelium of the cochlear duct which here forms a single layer of flattened cells. On one side the membrane joins the periosteum of the lateral wall of the bony cochlea at the upper end of the spiral ligament; on the other side it is attached to the vestibular surface of the lamina spiralis ossea near its free border. This leaves a part of the osseous spiral lamina in the boundary between the scala vestibuli and the ductus cochlearis. At the place where the vestibular membrane joins the periosteum of the osseous spiral lamina the latter is markedly thickened to form the *limbus (laminae) spiralis* or *crista spiralis* of dense, fibrous connective tissue containing many cells. This thickening has a free border or lip, the *labium vestibulare*, projecting into the ductus cochlearis. The part of the ductus cochlearis lying between the labium vestibulare and the lower lip or labium tympanicum is called the *sulcus spiralis (internus)*.

A similar but much greater periosteal thickening, the *ligamentum spirale* is found on the inner surface of the outer cochlear wall where the lamina basilaris is attached. The line of junction is known as the *crista basilaris*. This thickening in transverse section, has almost a crescentic form and extends toward the scala vestibuli as far as the attachment of the vestibular membrane and in the opposite direction as far as the scala tympani. It consists of numerous connective-tissue fibers and flat cells. Similarly there is a slight thickening along the line of attachment of the vestibular membrane, the crista membranae vestibularis. The epithelium of the ductus cochlearis covers the inner surface of the spiral ligament and immediately beneath this epithelium there lie numerous capillaries. Capillaries also appear to enter among the several layers of cells which compose the epithelium, forming a vascularized epithelium here known as the *stria vascularis*.

Pl 85, Fig. 2

The stria vascularis is bounded below toward the attachment of the lamina basilaris by a projection, the *prominentia spiralis*, which contains a small blood vessel. In man this prominence is often not very distinct in the upper part of the cochlea. The area between the spiral prominence and the lamina basilaris is known as the external spiral sulcus and is covered by a single layer of cubical epithelium.

The tympanic wall of the cochlear duct, *i. e.* the wall turned toward the scala tympani, shows two distinct parts; an inner, the limbus spiralis, nearer the axis of the cochlea and an outer, the basilar membrane. The former is attached to the osseous spiral membrane while the latter alone bears the organ of Corti.

Pl. 85, Fig. 3

The *limbus (membranae) spiralis* shows radial folds which project toward the labium vestibulare and are separated by distinct furrows. They are known as the AUDITORY TEETH OF HUSCHKE and their number is estimated as 2500. The epithelium of the cochlear duct is very flat where it enters the furrows between the auditory teeth and covers the surface of these structures. Resting upon the flat epithelium is a peculiar structure, the *membrana tectoria*, marked by fine radial striations and perhaps cuticular in origin. At the labium vestibulare it increases considerably in thickness and projects freely over the internal spiral sulcus to cover the surface of the organ of Corti. Its free border usually becomes somewhat thinner, bends upward and ends at about the region of the external hair cells (see below). Its under surface, turned toward the organ of Corti, is almost flat and lies so close to the hair cells as even to touch their hairs. The upper surface of the tectorial membrane is turned away from the organ of Corti and is strongly convex. At its base where it joins the limbus spiralis the membrane is thin, it then becomes thicker only to become thin again toward its free edge. The membrane appears distinctly marked by parallel lines and seems to consist of very fine fibrils held together by a gelatinous cement. It possesses a high degree of elasticity.

The organ of Corti proper lies between the internal and external spiral sulci on that surface of the lamina basilaris which is turned toward the cochlear duct. Both sulci are Pl. 85, Figs. 3, 4 covered by the simple cubical epithelium of the cochlear duct, which in the external sulcus has received the name "cells of Claudius"; while the epithelium of the organ of Corti is elaborately differentiated. Its connective tissue basis, the *membrana basilaris*, also shows various peculiarities. It forms the chief element of the lamina basilaris, and is a continuation of the periosteum of the osseous lamina and the tissue of the limbus spiralis; but consists entirely of straight, rigid, collagenous fibers in strikingly parallel arrangement stretched between the labium tympanicum and the spiral ligament. They are known as the AUDITORY STRINGS or fibers of Corti and their number is estimated as 24,000. Their length steadily increases from 100 μ in the basal turn of the cochlea to 500 μ at its apex, the breadth of the lamina basilaris increasing in like manner. On the other hand their thickness is everywhere the same, 1—2 μ. The fibers of Corti are very closely bound together or perhaps embedded in a common ground substance. Their nature is not thoroughly understood; they are too thick to be single collagenous fibers but may be fiber bundles. The parts of the fibers immediately beneath the organ of Corti show certain differences from the parts lying beyond it. In the latter zone the fibers and their arrangement as described above are most distinct. On the tympanic surface of the membrane lies a relatively soft connective tissue consisting of bundles of delicate connective fibers and spindle-shaped cells. Both the fibers and the cells of this connective tissue lie at right angles to the fibers of the lamina basilaris. This formation, known as the TYMPANIC INVESTING LAYER, encloses a small vein or capillary, the VAS SPIRALE. The upper layer of the membrana basilaris lying next to the cochlear duct is homogeneous, but in places contains nuclei.

The **organ of Corti,** *organon spirale*, consists of epithelial elements of very diverse kinds; but divisible, like the elements of the maculae and of the cristae, into sensory or Pl. 85, Figs. 3, 4 hair cells and supporting cells. To the latter class belong those cells known as the RODS OF CORTI. These are arranged in two spiral rows and are distinguished as the inner and the outer rods. They are peculiarly modified epithelial cells in which there has formed a fibrillar supporting substance, of apparently great powers of resistance and responsible for the unusual form of the cells. Inner and outer rods are bent toward one another (the outer being the longer are more inclined than the inner) and thus form the two sides of a triangular TUNNEL whose base is the membrana basilaris. This space steadily increases in both height and breadth toward the apex of the cochlea. The inner rods, *i. e.* those which are nearer the axis of the cochlea, consist of a broad foot-plate, a slender body and an expanded head. Upon the side of the foot-plate next to the tunnel is a small quantity of protoplasm in which the nucleus can be recognized. From the foot-plate rises the slender body which inclines slightly from the vertical, is distinctly striated, and consists chiefly of the supporting substance. Its upper end is expanded to form the so-called head which bears on its upper surface a broad, flat plate, the head-plate; while its surface turned toward the outer rod opposite to it is concave to receive the latter. This produces the appearance of a joint, but since the heads of the two rods are firmly united no movement is probable. In that border of the head-plate which is turned toward the axis of the cochlea there is a notch, into which is fitted the head-plate of the inner hair cells. Although longer, the outer rod resembles the inner, and its foot-plate similarly shows protoplasm and nucleus on that side of it which is turned toward the tunnel. The head is convex and fits into the concave socket of the inner rod, but is covered by the head-plate of the latter. In addition the head of the outer rod possesses a phalangeal process (see below). The broad feet and the heads of the rods, especially the head plates of the inner rods, are directly attached to their neighbors. On the other hand, between the slender bodies of the rods there are considerable intervals by which the tunnel stands in communication with the neighboring spaces. The number of the inner rods (6,000) is greater than that of the outer (4,500) so that from time to time one outer must articulate with two inner rods. The fibrillar supporting substance of the rods, although differing somewhat in different vertebrates, always consists of separate tonofibrils which in the thin, middle portions of the rod cells are so closely pressed together that the individual fibers can scarcely be distinguished. But toward the head and the foot they spread out in fanlike form. In many animals the head of the rod has in its interior a compact body apparently not of fibrillar nature.

The remaining elements of the organ of Corti are intimately connected with the rods, both the supporting cells or cells of Deiters as well as the so-called HAIR CELLS, which are the true sensory cells. The latter resemble the corresponding cells of the maculae and cristae. They are short and cylindrical while the base of each cell is rounded and does not extend quite to the basal membrane. The nucleus lies in the basal part of the cell;[1] Pl. 85, Fig. 3 above it is a threadlike structure, the spiral body of Hensen, and above this in turn, near the top of the cell is the centrosome — a diplosome. A cuticular border, like a lid, covers the surface of the cell, and bears 30—40 (at times even more) long, stiff hairs. A single row of inner hair cells is to be distinguished from 3—4 rows of outer hair cells. The inner hair cells are shorter than the outer hair cells and have a greater resemblance to those of the vestibular apparatus. They lie close against the inner surface of the inner rod cells, *i. e.* against the surface which looks toward the axis of the cochlea; while the outer hair cells lie external to the outer rods. The supporting cells of DEITERS intervene between the 3—4 rows of outer hair cells and between their innermost row and the outer rods in such fashion that no two rows of hair cells, nor even two hair cells of the same row, are in contact with one another. Because of the peculiar form of their upper, free ends the cells of Deiters are also termed PHALANGEAL CELLS.

The cells of Deiters form an inner row and three or four outer rows. They are long, Pl. 85, Figs. 3, 4 columnar cells, each with a broad base and a slender process at the upper end. The bases rest on a basal membrane and fit closely together. Each base contains a nucleus which usually is quite spherical. From this columnar, basal part of the cell a slender process extends upward between the hair cells to reach the surface of the epithelium. Here they end in a flat expansion, shaped somewhat like a dumbbell and termed the phalanx of the cell because of its resemblance to a digital phalanx. The phalanges fit together in such fashion that the adjacent concavities of any two neighboring phalanges of the same row form a space in which lies the top of a hair cell. The number of the cells of Deiters thus corresponds roughly to the number of hair cells, or is perhaps somewhat less since the tops of the inner row of outer hair cells involves the phalangeal processes of the outer rods.

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[1] But not quite at the base for beneath it there is a condensation of the protoplasm known as the nucleus of Retzius.

The outermost cells of Deiters probably pass without sharp boundary into the cells of Hensen. Throughout the whole length of a cell of Deiters there runs a stiff, solid fiber, known as the fiber of RETZIUS, which is prolonged into the phalangeal process.[1] This fiber appears compact in the slender part of the cell; but toward the base it splits up into diverging fibrils which, closely packed together, are the real components of the fiber of Retzius. Some of these supporting fibrils extend into a lateral process projecting from the upper part of the body of the cell. This process, like a cup, receives the rounded, basal end of a hair cell which thus obtains a firm support on the side of the cell of DEITERS.

As already mentioned the phalanges of the cells of Deiters are so arranged that the broad ends of the phalanges of neighboring cells lie in contact and are joined by a cement substance to form a framework. The tops of the hair cells with their sensory hairs Pl. 85, Fig. 4 are not merely accommodated but are firmly fixed in their phalangeal frames. The latter constitute the so-called *membrana reticularis*.

As previously mentioned the number of the supporting cells of Deiters corresponds to the number of outer hair cells; as a result the outermost supporting cells, those most distant from the cochlear axis, can each bear only a half-phalanx. Half-phalanges are also born by the heads of the outer rods, since they form the settings into which fit the heads of the hair cells of the first row. Each inner hair cell lies with its top in a frame formed in part from the notch in the head-plate of an inner rod (p. 288) and in part by Pl. 85, Fig. 3 the phalanx of an inner cell of DEITERS (limiting cell). The latter is that cell of the epithelium lining the spiral sulcus, which lies next to the inner rod.

Between the inner row of outer hair cells or the phalangeal processes of the first row of Deiters' cells and the outer rods there is a free space filled with endolymph, the so-called SPACE OF NUEL.[2] It is connected with the tunnel of the rods (see above). The outermost row of the outer cells of Deiters is in contact with epithelial cells which at first are high but steadily become lower, always retaining their columnar form. These are the so-called cells of HENSEN which gradually pass into the cubical cells of CLAUDIUS lining the external spiral sulcus (p. 287).[3]

The hair cells as the true sensory epithelium receive the terminations of the fibers of the *ramus cochlearis nervi acustici*. These fibers are the peripheral (or distal) processes of the bipolar cells of the *ganglion spirale* which like a band extends the length of the osseous spiral lamina. Although really dendrites these fibers receive a medullary sheath as they leave the nerve cells and enter the canals in the labium tympanicum of the osseous spiral lamina. The canals join to form a network and the bundles of nerve fibers form a corresponding plexus whose meshes show both acute and right angles. Leaving the plexus, the fibers emerge through numerous foramina which give the name habenula perforata to this part of the osseous spiral lamina.

The fibers now lose their medullary sheaths. Some continue their previous radial direction and cross the tunnel of the rods in which fine, non-medullated fibers may always be clearly seen. Others take a spiral course, but in two divisions, one of which lies under the inner hair cells while the other extends under the outer hair cells. Thus by an indirect spiral path the fibers, already exceptionally slender, reach the base of the hair cells and form around each a cup-shaped network of fibrils. From this network individual fibrils seem to penetrate into the body of the cell for a considerable distance.

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[1] Beyond the innermost cells of Deiters, which are joined by their processes to the inner rods, the adjacent epithelial cells (so-called limiting cells) are said to be transformed into supporting cells. The tops of the inner hair cells would then lie between the phalangeal processes of these two varieties of cells, just as those of the inner row of outer hair cells lie between the phalangeal processes of the outer rods.

[2] Similar but slightly smaller spaces lie between the separate hair cells and the phalangeal processes of the outer cells of Deiters and between the outermost hair cells and the cells of Hensen.

[3] The fibers of Corti shining through the cells of Claudius give to the part of the lamina basilaris covered by these cells the name of zona pectinata; while the part covered by the organ of Corti is known as the zona tecta. The former zone is devoid of vessels.

The ARTERIES of the labyrinth usually arise from the internal auditory artery as a single small branch, the *arteria labyrinthi*. In rare cases the latter may be a branch from the anterior inferior cerebellar artery, or it may be double. The arteria labyrinthi divides into two branches, the *arteria vestibularis* and the *arteria cochlearis communis*, the latter again divides into the *ramus vestibulo-cochlearis* and the *ramus cochlearis proprius*. The vestibular artery is distributed as a rule only to the utriculus and to the adjacent parts of the lateral and superior semicircular canals; rarely to the lateral and upper half of the sacculus. Its branches form a capillary network of wide meshes, which however are smaller at the cristae and maculae. The ramus vestibulo-cochlearis supplies a branch, the saccular artery, to the whole sacculus, utriculus and the semicircular canals in the same manner as the vestibular artery; but also sends a branch to the lower turn of the cochlea. The ramus cochlearis proprius supplies the remaining part of the cochlea, running with the cochlear nerve in the longitudinal canals of the modiolus. Its finer branches form capillaries in the spiral ganglion, in the lamina basilaris and in the walls of the scala tympani and scala vestibuli (stria vascularis, see page 286).

The VEINS of the labyrinth take a course different from that of the arteries. The *vena aquaeductus vestibuli* carries blood from the semicircular canals and from part of the utriculus and empties into the superior petrosal sinus. The blood from the remaining part of the utriculus, from the sacculus and from the bony walls and lower turn of the cochlea is carried off by the *vena aquaeductus cochleae*; while the third cochlear vein, the *vena spiralis modioli*, carries the blood from the remainder of the cochlea into the internal auditory vein. In so doing the vena spiralis modioli, lying in the pars membranacea, receives the blood from the capillaries of the lamina spiralis. The vena spiralis thus drains the blood from the lamina spiralis, while the radicles of the cochlear veins (which empty into the aquaeductus cochleae) receive their blood from the bony walls of the cochlea by way of the *vena spiralis*. The latter vein consists of two parts, vena spiralis superior and vena spiralis inferior, the former receiving blood from the upper turn and apical part of the cochlea, the latter from the basal turn and adjacent part of the middle turn of the cochlea. Their radicles begin as small veins in the prominentia spiralis and run beneath the wall of the scala tympani to unite with the vena spiralis beneath the spiral ganglion.

The internal ear has NO TRUE LYMPHATIC VESSELS since it is surrounded by wide lymph spaces, the perilymphatic spaces,[1] which stand in connection with the subarachnoidal space through the perilymphatic duct of the aquaeductus cochleae.

2. The Tympanic Membrane and the Middle Ear

The tympanic membrane belongs to both the external and the middle ears since its outer surface is covered by the greatly thinned lining of the external meatus and its inner surface by the mucous membrane of the tympanic cavity. The substance of the tympanic membrane proper consists of bundles of fibrous connective tissue which are arranged radially in the outer layer and circularly in the inner layer. The circular bundles gradually become fewer toward the center of the membrane where only radial fibers are present. Attachment to the bone[1] occurs through the annulus fibrocartilagineus, a thickening of periosteal connective tissue whose name is incorrect since no fibro-cartilage is present but only connective tissue with many elastic fibers. The fibrous bundles of the membrane are accompanied by cells like those of tendons, but also to a certain degree like those of the corneal lamellae and hence termed corpuscles of the tympanic membrane. Elastic fibers are almost lacking in the tympanic membrane itself.

On the outer surface of this thin connective-tissue foundation lies the cutaneous layer, stratum cutaneum, of the tympanic membrane, *i. e.* the extremely thin covering

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1) See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III.

derived from the skin. Over the greater part of the membrane the epidermis rests upon a very thin corium without papillae, and this connective tissue in turn rests upon that of the tympanic membrane proper. A heavier layer of connective tissue, like a true corium, is found near and around the blood vessels entering through the so-called cutaneous strand in which an even looser, subcutaneous layer can be distinguished. On its inner surface the tympanic membrane is covered by the greatly thinned mucous membrane, stratum mucosum, of the tympanic cavity. This consists of an extremely weak layer of connective tissue, the equivalent of a tunica propria, bearing a flat-cubical, non-ciliated epithelium. Toward the margin of the membrane the epithelium becomes higher and gradually takes on the character of the cubical ciliated epithelium of the adjacent parts of the tympanum (see below).

The pars flaccida membranae tympani, or Shrapnell's membrane, is an exception to the structure as described above. In it the tightly stretched fibrous bundles of the membrane are wanting so that the cutaneous and mucous layers with their thin connective tissue are in immediate contact and alone form this part of the tympanic membrane.

BLOOD VESSELS and nerves enter the tympanic membrane chiefly by way of the cutaneous strand along the manubrium of the malleus. A small artery runs in this strand to the posterior border of the manubrium and terminates there in vascularizing the cutaneous layer of the membrane by means of radiating capillaries. A small vein takes the same course, but the veins of the tympanic membrane also form an annular plexus at the margin of the membrane. This plexus primarily collects the blood from the capillaries of the mucous lining.

With the exception of lymph capillaries no lymphatic vessels seem to be present in the tympanic membrane.

The NERVES of the tympanic membrane enter along with the blood vessels through the cutaneous strand, but comparatively few nerves come from the side of the tympanic cavity. They form fine plexuses in several layers, the most superficial of which is in the epidermis itself. They terminate either in the connective tissue in special corpuscles which resemble Ruffini's corpuscles or within the epithelium in simple free endings or fine end-knobs.

The microscopic anatomy of the **tympanic cavity** is essentially confined to the features of its lining of mucous membrane which also covers the auditory ossicles, their ligaments etc. The mucous membrane is mostly very thin and almost entirely free from glands. The tunica propria is of very delicate connective tissue containing few elastic fibers; its covering is always a simple epithelium of variable thickness. For the most part this epithelium is flat or flat-cubical, rarely — as near the opening of the Eustachian tube — it ranges from cubical to columnar. In the latter case the cells bear cilia, structures which as a rule are entirely wanting on areas of squamous epithelium.

The auditory ossicles consist essentially of true bone but there are often remnants of cartilage matrix in their interior and a superficial layer of cartilage covers the surface of the joints,[1] the surface of the manubrium of the malleus, and the vestibular surface of the foot plate of the stapes. The ossicles also possess a very thin covering of the tympanic mucous membrane.

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[1] The condition of the two joints between the three ossicles is quite variable. In some cases meniscus-like structures occur in their interior; in other cases a true joint cavity is lacking; the joint being thus a synchondrosis.

The two muscles of the tympanic cavity consist of striated fibers most of which are very fine. In the musculus stapedius it is quite noticeable that the internal perimysium is very strongly developed and in the tensor tympani that a connective-tissue sheath, like an aponeurosis, surrounds the muscle.

As regards the tympanic BLOOD VESSELS four small arteries enter the mucous membrane and form a rather wide-meshed, capillary network; the veins also form plexuses in the mucous membrane. The LYMPHATIC VESSELS of the wall of the tympanic cavity lie deep and run in the periosteum.

The NERVES of the tympanic cavity form the tympanic plexus in which scattered nerve cells are to be found (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III). The manner of termination of the nerves is not yet definitely known.

The Eustachian Tube, *tuba auditiva*

The Eustachian tube consists of two portions, the one bony, the other cartilaginous. The mucous membrane lining the tube also shows important differences in these two parts. In general the mucous membrane of the bony part resembles in its structure that of the tympanic cavity; while that of the cartilaginous part resembles the pharyngeal mucous membrane. These resemblances to tympanum and pharynx increase toward the corresponding Pl. 86 ends of the tube. The essential difference in the mucous coat of the two regions is that it is devoid of glands and lymphatic formations in the bony portion; while by contrast the cartilaginous portion uniformly contains glands and diffuse lymphatic tissue is abundant, even small lymph nodules are present. Apart from the dissimilarities of the lumen,[1] the epithelium of the bony portion of the tube is quite thin, that of the cartilaginous part definitely thicker. The latter is a ciliated epithelium of several rows of cells and goblet cells are uniformly present. Such an epithelium is found in the respiratory tract and over most of the nasal part of the pharynx. The epithelium of the bony portion is of the simple columnar type near the opening into the tympanic cavity and then gradually becomes two-layered. Goblet cells are at first wanting but gradually appear toward the beginning of the cartilaginous part.

A considerable increase in the thickness of the mucous membrane of the cartilaginous part depents upon its content of glands, the *glandulae mucosae tubae auditivae*. These are mucous glands of tubulo-alveolar form and resemble the mixed muco-serous glands of the nasal cavity. The mucous coat of the cartilaginous part is rich in lymph cells which, near the pharynx, may form nodules, the *noduli lymphatici tubae auditivae*. A perfect solitary follicle is rare, in particular germ centers are almost always lacking. At the pharyngeal end of the tube adenoid tissue is so great in amount that it has been termed the tonsil of the tube. Where the cartilage of the wall is lacking submucous adipose tissue occurs. The cartilage of the tube is of the hyaline type near the bony portion; while toward the pharynx elastic fibers enter increasengly into its composition, its end, where the tube projects into the pharynx, being typical elastic cartilage.

The transformation of hyaline cartilage into elastic cartilage becomes almost complete in the course of time. In addition the connective tissue of the perichondrium penetrates into the cartilage, especially near its pharyngeal end, so that pieces of cartilage are more or less completely isolated; or the connective tissue by entering into the substance of the cartilage produces the characteristics of fibrocartilage.

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[1] See Sobotta-McMurrich. Atlas of Human Anatomy, Vol. III.

Blood vessels are abundantly present in the mucous membrane of the Eustachian tube. They form a capillary plexus just under the epithelium and a deep plexus around the glands of the cartilaginous part. The lymphatic vessels lie deeply and run in the periosteum. Nerves are rather abundant in the mucous membrane but the manner of their termination is not very well known.

3. The External Ear, *auris externa*

The external ear is composed of the auricle (pinna) and the external acoustic meatus. The **auricle** is a fold of the skin surrounding an elastic cartilage which shows the typical characteristics of this kind of tissue; viz. close networks of elastic fibers woven around the cartilage cells and passing directly into the perichondrium.

The skin of the auricle is almost everywhere devoid of fat and shows the characteristic structure of skin (p. 296) resembling particularly that of the neighboring parts of the face. It lies directly upon the cartilage to which it is intimately connected. The auricle has few sweat glands, in certain areas they may be altogether lacking; but large sebaceous glands accompany the fine lanugo hairs, which however are few in number. The integument of the auricle shows peculiarities in two places. First, the underlying cartilage is lacking in the lobule where its place in determining the form and size of the part is taken by the only subcutaneous adipose tissue in the auricle. Second, the inner surface of the tragus bears a group of quite stout body hairs, the tragi, which appear especially well developed in the male sex, but are not formed until adult life. The sebaceous glands belonging to these hairs are relatively small. There is no sharp boundary between these and the much finer hairs of the external acoustic meatus.

The common integument lines both the cartilaginous and the bony portions of the **external acoustic meatus** and extends over the outer surface of the tympanic membrane. Pl. 88, Fig. 6 This covering of skin diminishes in thickness toward the membrane, undergoing at the same time a marked reduction in its layers. The stratum corneum of the epidermis is very thin and the papillae of the corium, even in the cartilaginous portion, are very low and gradually disappear. Short and fine lanugo hairs and glands are found only in the thicker part of the lining present in the cartilaginous portion. Hairs and sebaceous glands are almost entirely absent from the bony portion. The so-called wax glands are present but sparingly and that only in the beginning of the bony passage.

The glands of the lining of the external meatus are in part large sebaceous glands, 2 mm. or more in diameter, belonging to the small lanugo hairs. The other glands are large apocrine sweat glands termed here ceruminous glands. They conform in structure to other apocrine sweat glands (p. 307) in having the secreting cells show varying heights according to the stage of secretion, while the width of the lumen in the coiled portion varies correspondingly but is always considerable. The ceruminous glands have one peculiarity not shared by the other apocrine sweat glands; their secreting cells, and particularly the rounded tops which separate during secretion, contain yellow or brown pigment granules of lipoid nature which are the cause of the yellow or brown color of the ear wax. From its consistency the latter must be essentially the secretion of the sebaceous glands of the external meatus, since the sweat glands here, as elsewhere, discharge a more fluid secretion. But the color of the wax depends upon the secretion of the ceruminous glands whose name is not entirely in error. The short ducts of the ceruminous glands are not sharply marked off from the coiled portions and discharge either independently, or into the ducts of the sebaceous glands.

The corium of the lining of the external acoustic meatus contains the glands. Neither adipose tissue nor a true subcutaneous tissue are present and elastic fibers are few or altogether lacking.

The cartilage of the external acoustic meatus is of elastic nature like that of the auricle, with which it is inseparably connected. Its perichondrium is firmly united to the skin. Vessels and nerves of the external ear show almost exactly the same relations as do those of the skin of other parts of the body, the resemblance is particularly close to the skin of the facial region.

XII. The Organ of Taste

Pl. 87, Figs. 3, 4
Pl. 43, Figs. 2, 3

The organ of taste consists of the **TASTE BUDS** embedded in the epithelium of the mouth cavity, chiefly in that of the vallate papillae of the tongue. To a lesser extent taste buds occur on the epiglottis and occasionally on the soft palate. In early years there are true taste buds on the papillae fungiformes but in adult life they are not present on the anterior part of the tongue. They are ellipsoidal in form, often almost barrel-shaped. The base of a taste bud is usually broad and rests close against the basal membrane of the epithelium, while the opposite end is narrowed and reaches almost to the free surface of the epithelium. The long axis measures about 75—80 μ and is always perpendicular to the surface of the epithelium; the breadth is about 40—50 μ. Where the apex of the bud touches the surface there is found a small pitlike depression in the epithelium, the taste canal or taste pore.

Two varieties of cells enter into the formation of a taste bud, sensory cells and **SUPPORTING CELLS**. The latter occupy the periphery of the bud and are long curved cells with the concavity turned toward the center of the bud so that they resemble barrel staves. Their basal ends are usually thicker than those turned toward the taste pore, but the reverse may be the case. These cells form several layers one inside another, the inner cells being less strongly curved than the outer. They have a spherical or ellipsoidal nucleus and a rather clear cell body. The sensory cells or **TASTE CELLS** are long, straight, spindle-shaped cells, thickened where they contain the nucleus, the nuclei being at different levels in different cells. They occupy chiefly the center of the bud, but are not as a rule in contact with one another, being separated by a few central supporting cells (so-called rod cells). The nucleus is always ellipsoidal, the protoplasm dark. The upper end of the cell is conical or cylindrical in form and bears a thick, highly refractive, peg-shaped, cuticular structure, the **TASTE HAIR**, which projects into the taste pore. The cells are consequently known as hair cells. The hair is stained brown by osmic acid and is colored intensely by eosin and by the use of gold chloride.

In addition to the crescentic supporting cells, in many animals there are large, branched supporting cells at the base of the bud, so-called basal cells. Tonofibrils have been observed in the taste (or supporting?) cells.

All the cells of a taste bud are firmly united by a cement substance.

Pl. 43, Fig. 2

The taste buds of the vallate papillae and of the papilla foliata, are innervated by **FIBERS OF THE GLOSSOPHARYNGEAL NERVE**. These fibres, which in the mucous membrane are associated with numerous small ganglia, enter the epithelium as medullated fibers but lose their medulla within it. In the branches which run to the taste buds there are certain fibers which terminate in the epithelium between the buds and are consequently known as intergemmal fibers. Others, known as intragemmal fibers, enter into the taste buds themselves. The neurofibrils of the former end in plexuses around the taste buds; while those of the latter form a fine network within the bud and a terminal network around the taste cells.

XIII. The Organ of Smell

The organ of smell is situated in the epithelium of the olfactory region of the nasal cavity (p. 222); consequently it is not enclosed as are the organs of the higher senses.

The epithelium of the olfactory region of the nasal mucous membrane within which the sensation of smell arises is relatively thin, varying from 30—60 μ (usually more in the newborn). It is distinguished from the immediately adjacent epithelium of the respiratory region, in the first place by the lack of cilia; however in man both kinds of epithelium extend, in places, beyond the bounds of the corresponding regions of the mucous membrane. Islands of mucous membrane of the olfactory type are found scattered in the respiratory region and islands of ciliated epithelium are found in the olfactory region, in which case the mucous membrane beneath often retains unaltered the characteristics of the olfactory region.

Pl. 55, Figs. 4, 5
Pl. 87, Figs. 1, 2

Essentially the olfactory epithelium consists of two different types of cells, sensory or olfactory cells, and supporting cells. The OLFACTORY CELLS are epithelioid cells of variable form; in places they are short and near the spherical nucleus, thick; in other places they are greatly elongated. Where the epithelium is very thick they are particularly long and slender, especially in the basal portion of the cell; they are not markedly thickened even opposite the ellipsoidal nucleus. The olfactory cells invariably extend through the entire thickness of the epithelium; but the nuclei are in several rows for they lie at different levels in the epithelium, although never close to the base nor to the free surface of the cells. The basal process of the cell is usually very thin. Narrowing still more to a threadlike form it penetrates the basal membrane of the epithelium and passes directly into a non-medullated fiber of the olfactory nerve. The olfactory cell must thus be considered a true nerve cell or neuro-epithelial cell, quite analogous to the neuro-epithelial cells of the retina (p. 271). The condition of the process of the olfactory cell which is directed toward the surface of the epithelium is not perfectly clear. It is stouter than the basal process and in the longer cells is almost prismatic and but little thinner than the part of the cell which contains the nucleus. It appears, at least in man, to project beyond the general level of the surface of the epithelium and to end in a fine conical process, the olfactory cone. There is found over the entire epithelial surface a membrane-like gelatinous (?) layer, into which the olfactory cones project. According to another view the true condition is not that of a cone but of a group of olfactory hairs or rods, as in the olfactory mucous membrane of many animals.

The SUPPORTING CELLS of the olfactory epithelium are in several rows and form a stratified columnar epithelium into which the olfactory cells are fitted. The ellipsoidal nuclei near the surface of the epithelium belong to the superficial columnar cells; the spherical nuclei next to the basal membrane are those of the basal cells; while the nuclei of the middle layers are those of both supporting and olfactory cells intermingled. As already noted the superficial columnar cells do not bear cilia. Terminal bars can be demonstrated between their ends; in this regard supporting cells in general resemble those of ordinary epithelium. Branched and pigmented figures are found between the epithelial cells similar to the figures of the bulbs of the hairs (p. 302). Here however, in accordance with the limited amount of pigment in the olfactory region, the figures are few and scattered.

Pl. 55, Fig. 5

XIV. The Skin, *integumentum commune*

Pls. 88—92 The skin, *integumentum commune*, consists of two principal parts: 1. the epithelial covering or *epidermis* 2. the connective tissue basis of the skin, the *cutis (derma)*. The latter is again subdivided into two portions which are not sharply separated, a dense superficial layer, the *corium* and the more loosely woven *tela subcutanea* or subcutis which connects the skin with the parts beneath and may contain adipose tissue.

Pl. 88, Figs. 1, 3–5 The **epidermis** is a stratified squamous epithelium, the upper layers of which are cornified. As a result two principal layers may be distinguished, the superficial horny layer, *stratum corneum*, and the deeper germinal layer, *stratum germinativum*. Where the epidermis is very strongly developed, as on the sole of the foot and the palm of the hand, the stratum germinativum shows four subdivisions. The deepest layer next to the boundary of the corium is called the *(sub-) stratum cylindricum*; then follows the greater part of the germinal layer, the *(sub-) stratum dentatum (spinosum)*, then the *(sub-) stratum granulosum* and next to the boundary of the corneous layer the *(sub-) stratum lucidum*. This subdivision is also that which is most favorable for the study of the epidermis. The cornified surface of the epidermis is comparatively smooth. On the other hand, that next to the corium is indented by cylindrical or conical projections, papillae, from the corium. Consequently the germinal layer of the epidermis is much thicker in the intervals between the papillae than it is over their apices.

1. GERMINAL LAYER, *stratum germinativum*.[1] The deepest layer in this subdivision of the epidermis is the *stratum cylindricum*. It consists of a single layer of columnar cells with elongated nuclei. In the pigmented skin of the colored races and in pigmented areas of the white races it is the most important seat of the pigment granules. The surfaces of the cells are in close contact with one another, apparently without a true intercellular Pl. 88, Fig. 5 cement being present. Actually a cement is present although fibers from the membrana propria penetrate between the basal portions of the cells.

The *stratum dentatum (spinosum)* forms the greater part of the germinal layer and consists of as many as ten layers of more or less flattened, polyhedral cells, the nuclei of which are approximately spherical. These cells are connected with one another by very distinct intercellular bridges (p. 31). The cells of this layer (prickle cells) fill the intervals Pl. 88, Fig. 3 between the papillae of the corium. The surface of the stratum dentatum consequently is Pl. 3, Fig. 13 smooth or almost so and is approximately parallel to the surface of the epidermis as a whole. The nearer the cells of the stratum dentatum approach to the corneous layer the more markedly flattened they become.

Next to the stratum dentatum there follow two to four layers of fusiform cells filled with irregular granules, thus forming the *stratum granulosum*. These granules stain with many dyes but most strongly with those which are basic[2] (basophile). They have been given the name of KERATOHYALIN but have nothing to do with the corneous material, the keratin (see below), since they are very different chemically and since cornification may take place (*e. g.* in the nails) in the absence of keratohyalin. In general the cells of this layer contain Pl. 88, Fig. 3 nuclei and like the cells of the stratum dentatum possess intercellular bridges.

The most superficial layer of the stratum germinativum, the *stratum lucidum*, forms a transition to the stratum corneum. It bears its name because of the marked translucency of its cells which apparently are non-nucleated and are arranged in two, or at most three, layers. Nuclei are not truly absent but are very greatly shrunken; consequently the stratum lucidum may be regarded as formed of cells which are already dead. As a rule cell boundaries are indistinct and intercellular bridges have ceased to exist. The cells of this layer are permeated by a diffuse, non-granular substance named ELEIDIN. This forms a membranous outer layer in each cell, indications of which were already present in the stratum granulosum. Eleidin appears invariably to be oxyphilic and represents liquified keratohyalin. This layer is almost completely confined to those areas of the skin in which the corneous layer of the epidermis predominates in thickness over the germinal layer.

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[1] Also termed the stratum mucosum of Malpighi. The cells of this layer easily become macerated and soft like mucus.

[2] But acid dyes are also taken up by the granules of keratohyalin although they show most affinity for basic dyes when a mixture of both kinds is used.

2. CORNEOUS LAYER, *stratum corneum*. This stratum consists of a variable number of layers of flat, cornified cells which in appearance, but not in reality, are devoid of nuclei. On the palm of the hand and the sole of the foot this layer is thicker than the stratum germinativum. The cells are usually greatly flattened, each cell consisting of a cornified, membrane-like, external layer with uncornified, shrivelled contents and a cavity containing the remains of the nucleus which has not as yet completely disintegrated. The horny material, KERATIN, is a relatively hard substance, extremely resistant and not attacked by most reagents, not even by strong acids. Pl. 88, Figs. 3, 5

While cornification may take place in the absence of keratohyalin, this substance is to be found only where true cornification is present. The views as to its origin have already been given. It is almost certain that it is not derived from the nucleus although it is markedly basophilic in the epidermis; however in the inner root sheath of the hairs — see p. 301 — it stains strongly with acid dyes. According to recent views it is produced by the disintegration of the epidermal fibers (tonofibrils, see below). However other materials of the cytoplasm probably add to the substance derived from the disintegration of the fibers and consequently share in the formation of the typical granules.

Eleiden represents keratohyalin in a liquified state; both substances probably are closely related to lipoids.

Impregnation by silver or gold reveals the presence of peculiar branched cells between the cells of the stratum germinativum of the epidermis. The significance of these cells, known after their discoverer as cells of LANGERHANS, is imperfectly understood. By many they are accepted as epithelial cells but others consider them connective-tissue cells in an intra-epithelial position. The former view connects them with the formation of pigment, the latter assumes for them a connection with the endothelial cells of the capillaries in the papillae of the corium.

Certain methods of staining easily reveal fibrils, so-called supporting or *tonofibrils*, in the cells of the epidermis within which they form a network of gently curving lines. The fibers run in part diagonally through the cell, frequently they have a tangential position. They reinforce the intercellular bridges between the cells of the stratum spinosum and are thus continued through several layers of cells. They are said to break up in the stratum granulosum forming the granules of keratohyalin and to become liquidified in the stratum lucidum, becoming again transformed into fibers at the boundary of the stratum corneum. Pl. 4, Fig. 6

It would seem that the cells of the stratum germinativum serve primarily to replace cells which are lost from the stratum corneum. That they have this power is beyond all doubt for even great losses of cells from the stratum corneum are made good through regeneration; a regeneration which can only proceed from the living cells of the deeper layers of the epidermis. In cases in which there has occurred considerable loss in the stratum corneum mitotic cell division may actually be seen, particularly in the stratum cylindricum; more rarely mitoses are to be seen in the stratum dentatum. The fact that commonly but few mitoses are to be found in the epidermis does not necessarily lead to the conclusion that replacement occurs through amitotic division, such as has been described in the stratum dentatum, since normally loss of cornified cells from the surface of the epidermis must occur only to a very slight extent.

It must be emphasized that the thickness of the corneous layer of the epidermis and the thickness of the germinal layer are in no way related to one another. Germinal layers of very considerable thickness are to be found just in those parts of the skin in which the corneous layer is very thin. The great development of the stratum germinativum of the epidermis, particularly in areas where the stratum corneum is thin, agrees with the fact that the epidermis is an organ of such vital importance that relatively small disturbances of function may result in severe injury to the body as a whole and may even cause death. It may perhaps also indicate that while the stratum germinativum shows a wide superficial distribution it may also act as an important GLAND OF INTERNAL SECRETION.

In areas in which the epidermis is thin the stratum lucidum is entirely absent or consists only of a frequently interrupted layer of cells. On the other hand the stratum granulosum is rather constant in occurrence, although often it consists of but a single layer of cells. Thus in the skin of the face there is present a well formed stratum granulosum along with a poorly developed corneous layer. In most regions of the skin the stratum corneum
Pl. 88, Fig. 5 is thinner than the stratum germinativum and by fusion of neighboring cornified cells often forms distinct lamellae, a process which does not occur in a thick corneous layer.

In regions of the body in which the skin is dark in color (anus, genitalia, nipple) and still more in the colored races of man, fine pigment granules (melanin see p. 15) are found in the deeper layers of the stratum germinativum, particularly in the stratum cylindricum.

The **corium** consists essentially of a dense feltwork of interwoven connective-tissue
Pl. 88, Figs. 1, 3 bundles. It may be subdivided into two layers of different texture, which, however, are not
Pl. 5, Fig. 3 clearly defined; 1. the *stratum papillare*, consisting of delicate connective tissue containing
Pl. 6, Fig. 3 very fine elastic fibers and also fibers of reticulum; 2. the *stratum reticulare*, a deeper layer with typical interwoven connective-tissue bundles among which are strong networks of moderately thick elastic fibers. The thick collagenous bundles which compose the stratum reticulare of the corium are, for the most part, strictly parallel to the surface of the skin; at least the angle which they form with the surface is always an acute angle and consequently the network is one of rhombic meshes. The elastic fibers follow the chief strands of the collagenous fibers and, as always in the body, form networks which are particularly close around the sebaceous glands.[1] In addition to the usual fibrocytes, mast cells are uniformly found in particular abundance. Towards the epidermis there appears an unusually delicate feltwork of reticulum fibers which presents an exact, negative picture of the superimposed epidermis. Its outermost fibers extend between the basal ends of the stratum cylindricum; consequently the stratum papillare of the corium is made to adhere to the epidermis.

Pl. 88, Fig. 3 The papillae of the corium are formed essentially by the stratum papillare; their number, size and arrangement varies greatly in different regions of the skin. Capillary loops are always to be found in the connective tissue of the papillae and frequently they are accompanied by tactile corpuscles. In the palm of the hand and the sole of the foot the papillae are especially long (up to 0.2 mm.) and in general the length of the papillae is directly connected with the degree of development of the stratum corneum of the epidermis. However the papillae of the margin of the lip are very long while those in the skin of many regions of the trunk are but poorly developed. The long papillae of the palm of the hand and the sole of the foot are arranged in two parallel rows, thus producing the so-called cutaneous ridges of these regions.

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[1] Naturally the corium shows regional differences in its structure. These concern particularly the elastic fibers which here and there form two distinctly separate networks, one of which is sub-epithelial and the other much deeper in position. In the skin of the face there occur networks of broad band-like fibers knotted together in a distinctive fashion.

In certain areas of the skin the corium contains smooth muscle, but much less abundantly in man than in most animals. Erector muscles (p. 303) are constantly associated with the majority of the hairs, but smooth muscle also occurs independently of the hairs. This is always the case in the skin of the scrotum (tunica dartos), in the nipple and its immediate neighborhood, less uniformly in other parts of the skin of the male genitals (praeputium, glans penis, skin of the perineum) and occassionally in other places (axilla, cheeks, back and extremities). Striated muscle is only occasionally found in the corium, as in the face where the ends of the mimetic muscles extend into this layer of the skin. The smooth muscles of the skin invariably end in elastic tendons and the striated muscle of the face shows the same peculiarity. Although in man the true pigment of the skin lies in the epidermis, small quantities of pigment are to be found in the human corium and in animals the corium is found very commonly the seat of pigmentation. In general pigment cells are most frequently in the corium of those areas in which the epidermis is also pigmented, but as already noted neither uniformly nor in any considerable amount; nor does a marked relationship exist between the pigment of the epidermis and that of the corium. In the newborn of all races (not of the mongolian race alone) there is present a diffuse concentration of pigmented connective-tissue cells in the corium of the skin of the sacral region, producing the so-called MONGOLIAN SPOT.

The pigment cells of the Mongolian spot are situated in the deeper layers of the corium and are true cutaneous pigment cells containing melanin which has been formed in the cells themselves and which, like the pigment of the cells of the epidermis, gives the so-called dopa reaction (p. 17). On the other hand it is said that other corial pigment cells do not give this reaction and consequently they are regarded by many merely as cells which are transporting pigment (p. 17).

The **subcutaneous tissue**, *tela subcutaneae*, the deepest layer of the skin, unlike the corium consists of loose connective tissue. Throughout the greater part of the skin there is Pl. 88, Fig. 1 developed in this layer an abundance of adipose tissue, the so-called panniculus adiposus, Pl. 89, Fig. 2 but certain areas of the skin such as the eyelids, scrotum, penis, labium minus, pinna, etc. are free from fat. Even where the formation of adipose tissue is most pronounced, as in the scalp and in the palm of the hand and sole of the foot, there still remain strands of connective tissue, retinacula cutis, which separate the individual parts (lobules) of the mass of adipose tissue. As a result the boundary between corium and tela subcutaneae is not sharply defined.

The BLOOD VESSELS of the skin are very abundant, the larger branches of the arteries lie in the subcutaneous tissue and from there supply the corium in whose deeper layers there is formed the cutaneous plexus. From the latter finer branches pass upward to the papillae at the base of which they form the subpapillary plexus. From the deeper side of the cutaneous plexus recurrent branches supply the panniculus adiposus and form the capillary Pl. 88, Fig. 2 networks of the sweat glands and of the lobules of adipose tissue. From the subpapillary plexus there proceed the delicate precapillary arterioles which no longer anastomose but form capillary loops in the papillae of the corium. The stratum reticulare contains few capillaries.

Similarly the veins form a subpapillary plexus which, after only a short interval, is followed by a second superficial plexus. A third venous plexus is situated in the deeper layers of the corium and receives also the veins of the subcutaneous tissue; while the veins of the sweat glands ascend to reach the subpapillary plexus. Finally in the deeper layers of the subcutaneous tissue there is formed the fourth (subcutaneous) venous plexus, the larger trunks of which frequently bear the special name cutaneous veins.[1]

The LYMPHATIC VESSELS of the skin are very abundant and form a fine plexus in the corium and a coarser plexus in the subcutaneous layer. The former begins as capillaries with blind ends partly in the stratum papillare but particularly within the papillae themselves. Other such capillaries are present in the corium and around the coils of the sweat glands.

The skin, particularly the skin of the palm of the hand and the sole of the foot, is exceedingly rich in NERVES. The larger trunks form a plexus in the deeper parts of the subcutaneous layer and supply medullated fibers to the lamellar corpuscles which are so abundant in this region. The corium contains other plexuses, of which the most superficial lies at the base of the papillae. From the latter plexus nerve fibers run to the tactile corpuscles and others have intra-epithelial terminations (p. 179). For the most part the cutaneous nerves contain medullated fibers but non-medullated, sympathetic fibers are present to supply the blood vessels and sweat glands.[2]

Appendages of the Skin

In all of the three chief layers of the skin there are found special structures which by their development are derived from the epidermis. These are the hairs, the nails and the glands of the skin.

1. The Hairs

The hairs, *pili*, are long cornified threads projecting beyond the surface of the skin. Pls. 89, 90 Within the skin they are inserted in an uncornified epithelial (epidermal) sheath which in turn is surrounded by a sheath formed from the connective tissue of the corium. The portion of the hair embedded in the skin is known as the root of the hair (*radix pili*); the portion projecting freely beyond the skin is the shaft of the hair (*scapus pili*). The root of the hair terminates in a bulb (*bulbus pili*). The latter is invaginated by a connective tissue papilla which contains blood vessels and in the case of the lanugo hairs lies in the corium. The stouter hairs have their papillae in the subcutaneous layer since their roots attain a considerable length.

The epidermal sheath of the root of the hair is termed the ROOT SHEATH, while the connective tissue sheath is known as the HAIR FOLLICLE. The structure of a hair and its sheaths is shown best in the stouter hairs of the body.

The HAIR ITSELF **(the shaft of the hair)** has three chief components: the cuticle of the hair,[3] the cortex and the medulla. Of these only the first two are constantly present; the medulla may be lacking. The CELLS OF THE CORTEX form the chief bulk of the hair. They Pl. 90, Figs. 4–8 are long, fusiform, cornified cells containing both diffuse and granular melanin pigment and lie with their long axes parallel to the axis of the hair. In the lower part of the root of the hair they are somewhat shorter. According to the color of the hair the pigment granules are pale or dark, few or numerous. In very blond hair granular pigment is practically absent. The nuclei of the cells are elongated (less so in the lower part of the hair) and in the shaft of the hair which projects freely beyond the skin they have died and are represented by a vacuole. The cortical cells of the hair which usually are firmly attached to one another may be isolated by heating in caustic soda or concentrated sulphuric acid. Their long spindle-shaped form is then clearly displayed as is also their fibrillar structure.

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[1] See Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III.

[2] As to the vessels and nerves of the hairs, nails and glands of the skin see the sections on the parts in question.

[3] The term "epidermicula" would be better.

When present in the hair the MEDULLA forms a central axis consisting of large, polygonal, nucleated cells which are almost invariably unpigmented[1] and are usually arranged in one or two, rarely in three, rows. In and between the cells, particularly in the hair of adults, there are found small air cavities which are always intercellular[2] and which are also present in the cortex. They contain granules which are tinged by acid dyes. Pl. 90, Figs. 2, 4

The **cuticle** (or better epidermicula) **of the hair** consists of flat cornified cells bounded by wavy lines and overlapping like the tiles of a roof. In profile view they appear as flat teeth, like those of a saw, with their points turned toward the apex of the hair. In the lower part of the root they contain nuclei which later are lost and the cells then become approximately rectangular, non-nucleated scales which cover the shaft of the hair proper. Pl. 90, Figs. 1, 2, 4

The ROOT SHEAT of the hair consists of two parts, the so-called inner and outer root sheaths. However, the inner reaches only to the mouth of the glands of the hair follicle (see below).

The **inner root sheath** consists of two or three distinct layers; an inner layer (of Huxley), an outer layer (of Henle), and a sheath cuticle which forms the boundary next to the cuticle of the hair but which is distinct only in the deeper part of the root. By development the root sheath belongs to the hair itself and originally surrounded the latter to its apex; but in the fully developed condition of the hair it extends only to the opening of the sebaceous glands (see below). Its structure varies at different levels in the root of the hair. All three layers of which it consists may be clearly observed in its middle and lower parts. Pl. 89, Fig. 3 Pl. 90, Figs. 1, 2

The SHEATH CUTICLE forms the innermost layer of the inner root sheath. It resembles almost exactly the cuticle of the hair *i. e.* it consists of cornified scales which in the lower part of the root sheath still contain nuclei. Like the cells of the hair cuticle they overlap in the manner of tiles. However their free borders are turned towards the papilla of the hair, consequently they interlock with the scales of the hair cuticle which project in the reverse direction. The cuticle of the sheath terminates just above the middle of the root of the hair. The next layer externally is known as HUXLEY'S layer. It is formed of a single row of cubical or low columnar cells which in the lower part of the root of the hair contain numerous granules. These granules, so-called trichohyalin, resemble eleidin and stain lightly with basic aniline dyes but intensely with acid dyes. Their behavior is thus rather different from the keratohyalin of the stratum granulosum of the epidermis. The outermost (HENLE'S) layer is formed of flat cells which are almost always devoid of nuclei. Only in the deepest part of the root of the hair, immediately above the bulb, do these cells of Henle's layer contain nuclei and scattered granules of trichohyalin. The upper portion of the inner root sheath is of more simple structure being completely cornified and lacking a cuticle, while Huxley's and Henle's layers are fused together into a homogeneous mass which terminates in an irregular fringe.

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[1] In very heavily pigmented hairs a few pigment granules may be found in the cells of the medulla.

[2] White hairs contain an abundance of air, but pigment is largely wanting. The small air spaces appear black by transmitted light and white by reflected light.

Pl. 89 The **outer root sheath** repeats almost exactly the structure of the stratum germin-
Pl. 90, Figs. 1, 2 ativum of the epidermis into which it is continued without demarcation. It represents an invagination of the epidermis and shows traces of the stratum corneum and stratum granulosum as far as or beyond the mouths of the sebaceous glands. It consists of a variable number of layers of cells, the outer of which are columnar, the middle polyhedral and the inner of flattened polyhedral form. The latter border on the inner root sheath. In the deeper part of the root of the hair the number of layers of cells is less than in the upper part where the root sheath is thicker. Where the hair penetrates the epidermis the outer root sheath passes without interruption into the stratum germinativum; the cells of which do not show mitoses so frequently as do those of the outer root sheath. To the outer root sheath belongs also the so-called epithelial hyaline membrane (see footnote below).

The outer root sheath extends downward into the territory of the **bulbus pili** only
Pl. 89, Fig. 2 as far as the neck of the papilla. The layers of the inner root sheath may also be followed
Pl. 90, Figs. 2, 3 to this point where they all, including Henle's layer, pass into a mass of nucleated cells. The two root sheaths fuse with one another and since their cells are quite similar they form a mass whose elements are neither pigmented nor cornified. This mass surrounds the lowest part of the papilla of the hair and is thus the most external portion of the bottom of the bulbus pili, and is in immediate contact with the connective tissue papillae. Lack of pigment distinguishes these cells from the cornified cells of the bulbus which surround the more apical part of the papilla. They represent the matrix for the growth of the hair in length and always show mitoses.

The upper end of the bulbus pili is formed of cells which are already cornified and is
Pl. 90, Fig. 3 distinguished by its great abundance of pigment. In particular there are to be found here branched pigment figures which look as though melanoblasts[1] had migrated into the epithelium. Probably they are intercellular deposits of pigment.

The connective-tissue sheath of the hair, the **hair follicle,** *folliculus pili*, is only to
Pl. 89, Fig. 3 be observed in the case of the stouter body hairs and is entirely absent from the lanugo
Pl. 90, Figs. 1, 2 hairs. It consists of an inner, structureless, hyaline membrane which in the case of most of the stouter body hairs attains considerable thickness. Next follow connective-tissue bundles arranged in the form of a layer of circular fibers, while externally there is the layer of longitudinal fibers. The latter layer alone contains elastic fibers. The hyaline membrane[2] consists of reticulum fibers and is thus a kind of basal membrane.

As regards BLOOD VESSELS, the hair in the narrower sense, *i. e.* the epidermal structure proper, is non-vascular. Only the papilla and the outer layers of the connective-tissue hair follicle contain capillary loops. The NERVES of the hair likewise lie in the hair follicle, but not in the papilla which contains no nerves, or at most only vaso-motor nerves. The strongly developed sensory nerves of the hair follicle provide, particularly in many animals, for the sense of touch and in part form encircling plexuses about the hair while other fibers, losing their medullary sheath penetrate to the hyaline membrane where they become terminal fibers and run courses parallel to that of the hair. Fine fibers are said to penetrate the hyaline membrane and reach the outer root sheath between the cells of which they terminate.

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[1] See also p. 17. This appearance has been instanced in support of the migration theory and has also been associated with the cells of Langerhans.

[2] The hyaline membrane possibly consists of two layers. The outer and thicker layer, which is not always homogeneous but often appears to be finely striated, is of connective-tissue (reticulum fiber) origin. The inner layer is decidedly more delicate, is homogeneous throughout and is probably a cuticular secretion of the outer root sheath and consequently of epithelial origin. It is perforated by delicate pores.

The hairs are set obliquely in the skin, not perpendicularly to its surface; although in this regard and generally in regard to the shape of the hair and its root there are considerable racial differences. In general there is an acute angle at one side of the hair Pl. 89, Fig. 2 and an oblique angle on the opposite side. In the case of all lanugo hairs and of the hairs of the head, as well as many of the stronger body hairs,[1] the obtuse angle is crossed by a smooth muscle named the *arrector pili*. This muscle arises by one or more elastic tendons in the upper layers of the corium, close beneath the papillae and runs obliquely across the obtuse angle to the hair follicle in to which it is inserted at, or a little above, the middle of the root of the hair. At or near the point of insertion there is commonly found an evagination Pl. 89, Figs. 1, 2 of the follicle and outer root sheath of the hair. The sebaceous gland lies in the acute angle formed by the *arrector pili* and the hair, as a result the muscle acts not only as an "arrector pili" but still more as an "expressor sebi".[2]

The stronger body hairs are not isolated but stand in groups, so-called hair rings, which usually consist of three or four, (in rare cases of two or six) hairs.[3] This point constitutes a fundamental distinction between the stronger body hairs, which form groups and are placed close together, and the lanugo hairs which always occur singly. In their essential structure the latter resemble the stronger body hairs but are smaller, although they have remarkably large sebaceous glands and correspondingly large erector muscles.

2. The Development and Regeneration of Hairs

Hairs may be formed anew not only during embryonic life but throughout the whole period from birth to extreme old age. The manner of development of the hairs as it may be observed from the third month of embryonic life onward is essentially similar to the process by which hairs are replaced in the adult; consequently the development of the hair should first be briefiy reviewed. The formation of the hair begins as a local growth of the embryonic epidermis into the mesenchyme beneath. At the deeper end of this growth there appears early an accumulation of connective-tissue cells, the anlage of the papilla of the hair, which soon becomes grown over and surrounded by the thickened blind end of the ingrowing epidermis, thus forming the anlage of the bulbus pili. The mass of epithelial cells lying next the papilla (hair cone) forms the anlage of the hair and of the inner root sheath into which it is continued, while the remaining cells develop into the outer root sheath. The hair itself consequently grows from below upward while the outer root sheath on the other hand grows from without inward.

While the growing hair is yet very short the presence of pigment serves to distinguish it from the anlage of the inner root sheath in which no pigment is formed. It then becomes surrounded from its apex downward by the gradually cornifying inner root sheath. Before the young hair reaches the surface of the skin and breaks through to the outside there forms a canal, the HAIR CANAL, into which the inner root sheath leads. This canal arises by cornification and probably by subsequent disintegration of the axial cells of the epithelial cord and at first is closed. Later the cells over the cornified apex of the hair disappear so that the latter can emerge.

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[1] Erector muscles are lacking in the eyelashes and eyebrows, the vibrissae of the nostrils, and most of the hairs of the head, particularly those of the chin; but not in the hairs of the axilla, although in the latter case, as well as in some hairs of the beard they are but poorly developed.

[2] The muscle also appears to be a factor in the tone of the corium and in the vigor of its circulation.

[3] This applies to Caucasians. In this regard there are considerable variations among the different races of man.

During the differentiation of the whole epidermal ingrowth there have been produced two evaginations, one above the other, of which the upper represents the anlage of the sebaceous gland of the hair while the lower marks the region of attachment of the erector muscle. These evaginations lie in the obtuse angle.

The formation of the erector muscle, like that of the hair follicle itself, proceeds from the embryonic connective tissue which surrounds the epidermal ingrowth.

When a new hair replaces one which has fallen it is formed by a process quite similar to that by which the first hairs are formed in embryonic life. This **replacement of the hair** Pl. 89, Figs. 1, 2 occurs even in the embryo, each hair having a brief life, the duration of which is highly Pl. 83, Fig. 4 variable in the case of different hairs. It is shortest in the eyelashes, which live but a few weeks (4—6) and is longest, on an average four years, in the hairs of of the head, particularly those of females. But the ordinary lanugo hairs have only a life of little more, or even of less, than one hundred days.

The replacement of human hairs occurs in such a manner that only a single hair, usually but one of a group (p. 303), is affected at one time. The death of the hair occasions its fall and begins first by a loss of their power of increase on the part of the matrix cells of the bulbus pili, as a result of which further growth of the hair ceases. The entire bulbus gradually becomes cornified (see below), rises away from the papilla and becomes a solid club; that is to say it is no longer invaginated by a papilla. From a living papillary hair it has become a dead club-hair.

This cornification of the club-hair proceeds quite gradually and is not completed until the falling hair has been moved upward to the level of the insertion of the erector muscle. At first the clublike mass consists of uncornified cells and stands in connection by an uncornified strand of epithelium with the papilla which has shrunken greatly following the detachment of the hair. Later the epithelial cord represents a direct prolongation of the empty outer root sheath (see below).

The club-hair gradually becomes cornified and with its root sheaths is pressed upward towards the surface of the skin, at first only to the level of the insertion of its muscle. During this process the inner root sheath becomes largely cornified, the outer root sheath becomes empty and, like the hyaline membrane, is thrown into folds. It forms an empty epithelial tube[1] lying between the point of muscular insertion and the shrunken papilla. The hair follicle degenerates beneath the papilla which is becoming very small and now appears in the form of an insignificant strand of connective tissue, the so-called hair-pedicel.

As mentioned, the cornification of the club-hair is only completed when the latter has reached the level of the muscular insertion. As a rule the lower end of the club then breaks up before the hair is entirely expelled.

The club-hair remains at the level of the insertion of the muscle, embedded in the uncornified mass of cells until such time as the greatly shrunken papilla gives rise to the Pl. 89, Fig. 2 replacing hair and the latter crowds the old hair out. During this process the papilla rises to the level of the insertion of the muscle. The young hair is now formed from the material of the outer root sheath in essentially the same manner as the embryonic hair was formed from the indifferent cell mass of the original epidermal ingrowth.

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[1] The views on the process by which a hair is replaced have been in conflict and are not as yet completely in accord. Thus it is accepted in many quarters that the replacing hair forms a new papilla.

The young, replacing hairs are naturally at first much thinner than the perfected hair and may consequently be recognized at once by their slenderness. In addition they do not extend nearly so far into the skin since it is only in their later growth that they occupy fully the old hair follicle and attain the length of the old hair.

On the other hand the club-hairs and their sheaths, as well as their papillae, are found in a more superficial position within the skin than the papilla-hair, for after the separation of the hair its from papilla there occurs a marked shortening of the hair root. Whether contractile elements play a part in the later process is uncertain.

In addition to this replacement of hairs there appears to occur, although to a much less extent, a new formation of hairs by the epidermis after the manner of the formation of embryonic hairs.

3. The Nails, *ungues*

The NAILS are cornified epidermal plates which rest on an uncornified layer (stratum germinativum) in such fashion, that the horny plate of the nail proper corresponds to a very thick stratum corneum; while the proximal part of the germinativum represents the true matrix of the nail. Pl. 91, Figs. 1–3

The stratum germinativum of the nail rests in turn upon the so-called nail-bed[1] which is a modified corium.

The cornified nail consists of completely cornified cells which lie in closest contact with one another but which still show traces of a nucleus and in addition contain small air spaces, particularly near the margo occultus where their presence forms the lunula. The latter appears white to reflected light but is opaque to transmitted light. The germinal layer of the nail consists of the same elements as form the stratum germinativum of other areas of the skin and lies directly beneath the mass of cells which form the cornified nail. There is no more than an indication of stratum lucidum or stratum granulosum in the region of the nail proper. Over the greater part of the region of the stratum germinativum unguis, *i. e.* as far as the anterior part of the lunula, the high ridges of the nail-bed (see below) press into this layer. As a result, papillae are here lacking, and appear only in the neighborhood of the posterior part of the lunula; that is to say in the region of the nail matrix proper. Even here they are poorly developed. In contrast to the true nail a stratum granulosum is readily observed in the so-called eponychium (see Sobotta-McMurrich, Atlas of Human Anatomy, Vol. III).

The corium of the nail bed is distinguished by highly vascular longitudinal ridges which extend deeply into the stratum germinativum of the nail; toward the root of which they gradually become lower and give place to a few true, but irregularly formed, papillae. It is always free from adipose tissue and is formed of very compact bundles of fibrous connective tissue which are attached directly to the periosteum of the tuberositas unguicularis of the phalanx through which by means of Sharpey's fibers it is attached even to the bone itself.

As regards the BLOOD VESSELS of the nail bed there is a dense capillary network in the ridges, LYMPHATIC VESSELS are also present and numerous NERVES which terminate in the epithelium. Coiled and encapsuled nerve endings and Golgi-Mazzoni corpuscles are present in the corium of the nail bed.

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[1] The nomenclature varies; many writers give to the germinal layer of the nail the term nail-bed while others use the term hyponychium.

4. The Glands of the Skin

Pl. 91, Figs. 4–6
Pl. 92

The GLANDS OF THE HUMAN SKIN have long been divided into two chief classes; first the sebaceous glands or glands of the hair follicles, *glandulae sebaceae*, and second the coiled or sweat glands, *glandulae sudoriparae*.[1] In addition there is the mammary gland which will be considered separately. This classification which in many regards is quite antiquated, will here be followed upon didactic grounds; especially as hitherto no agreement on any other subdivision has been possible.

Pl. 88, Fig. 6
Pl. 89, Figs. 1, 2
Pl. 92, Figs. 7, 8
Pl. 75, Fig. 4

The **sebaceous glands,** *glandulae sebaceae*, occur as appendages of the hair follicles and always lie in the upper layer of the corium. In certain regions of the body they are found independently of hairs, so-called free sebaceous glands as in the labia minora, the red margins of the lips, the glans penis and praeputium; and to some extent with extremely fine lanugo hairs in the skin of the cheeks, in and near the nipples, in the transition zone between the skin of the alae nasi and the mucous membrane of the vestibular region, and that between the anal skin and the rectal mucous membrane. The ceruminous glands of the external auditory canal and the so-called glands of Moll belong to this category of sebaceous glands. All these are simple alveolar glands, either branched or unbranched, whose short, wide ducts discharge into the hair follicle or around the finer hairs. Generally it is the finer hairs that have large sebaceous glands, those of the larger body hairs being small; the largest sebaceous glands by far are those which occur independently of hairs. Similarly the number of glands is only two in the case of the stouter body-hairs and those of the head, while other hairs have more than two glands. Duct and gland together represent a direct continuation of the external root sheath of the hair.[2] The stratified squamous epithelium of the root sheath passes gradually into the epithelium of the gland.

Pl. 92, Figs. 7, 8

The alveoli of the glands do not possess a true lumen but are quite filled by their own cells. The latter are cubical and small at the periphery of the alveolus, but toward its center become increasingly larger and more vacuolated by the formation in the protoplasm of droplets of lipoid secretion. At the same time as the droplets increase the nucleus shrivels, becomes pycnotic and indented, so that the cells lying in the center of the alveolus consist of only a negligible nuclear remnant and a mass of fat droplets, the remains of the vacuolized cell-body still surrounded by a membrane. The secretion, sebum, is thus formed by the degeneration of the cells of the gland. Replacement of the degenerated cells is effected through the peripheral cells in which mitotic nuclear division may be found. The gland thus belongs to the holocrine group (p. 44).[3]

In the alveoli of the sebaceous glands, especially in those of larger size, there are always present strands of epithelial cells, like septa or trabeculae, which usually have a radial arrangement. These cells are for a time unaltered but subsequently may become converted into sebum.

A connective-tissue capsule, continuous with the follicular sheath and especially rich in elastic fibers, surrounds each sebaceous gland. The size of the glands varies between 0.2 and 2 mm., the largest are usually those of the alae nasi. Sebaceous glands are entirely wanting only on the palm of the hand and the sole of the foot.

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[1] Even in man this division does not correspond to the actual conditions and it is scarcely more useful for the cutaneous glands of many animals. In spite of this it is still of service in classifying the human cutaneous glands.

[2] Later the hair may be lost and the gland appear isolated.

[3] Occasionally in a few cells of an alveolus cornification occurs instead of the formation of secretion.

The **sweat glands**, *glandulae sudoriparae* (glomiformes), are long, simple tubular glands, whose blind ends are elaborately coiled and as a rule are unbranched.[1] The coil is the only secreting part of the gland; the DUCT is variable in length and runs a course which is straight or somewhat winding. Sweat glands are present in all regions of the skin although their size as well as the density of their occurrence is subject to wide variations. They stand closest together in the palm of the hand and the sole of the foot; in many areas of the body their number is scarcely half so great. Pl. 88, Figs. 1, 6 Pl. 89, Figs. 1, 2 Pl. 91, Figs. 4–6 Pl. 92, Figs. 1–6

Three types of sweat glands can be distinguished in man according to their form, size and finer structure or mode of secretion: APOCRINE and ECCRINE glands, the latter being again subdivided into those which are small and short, and those which are long.

As already mentioned all three types have in common the subdivision into two functionally different parts, the coil which alone represents the secreting part of the gland and the straighter, or occasionally spiral, duct. The coil has as a rule the form of a more or less flattened ball or irregular cone which, in the APOCRINE type of gland is large and stout. Glands of this type are found in the axilla, in the skin immediately surrounding the anus, and are scattered in the scrotal skin; to this category belong also the ceruminous glands of the external auditory canal and the so-called glands of MOLL of the eyelid. The coiled portion of these glands is long and of large diameter in contrast to the short and narrow duct which runs a straight course.

The cells of the ECCRINE sweat glands remain intact while producing their secretion (see below) which is much more watery than that of the apocrine type. Among them the long glands of the palm of the hand and sole of the foot are to be distinguished from the shorter glands of the rest of the skin. The latter have a very small coil the caliber of whose lumen is scarcely greater than that of the duct, which like that of the large apocrine glands, is short and almost straight. The glands in the palm of the hand and sole of the foot not only stand very close together but extend much deeper into the skin than do those of the other two categories. They are the only glands of the skin whose coils lie in the subcutaneous layer, even the large apocrine glands at the most reach only the boundary between the subcutaneous layer and the corium. Since the ducts of these glands of palm and sole are long and serpentine in course, penetrating the unusually thick stratum corneum in cork-screw fashion, these are the longest of all the sweat glands.

The structure of the coiled part of the sweat gland is studied best in the large **apocrine** glands in which it is most distinctly pictured; after it has been examined it is easy to understand the departures in structure among the eccrine forms. The caliber of the lumen of the coil changes greatly according to the degree in which the latter is filled by secretion; when empty it is small and the wall correspondingly thick, when full the lumen is wide and the wall thinner. The latter consists of two layers of cells, an inner of unbroken epithelium and an outer discontinuous layer of myo-epithelium. Pl. 91, Figs. 5, 6 Pl. 92, Figs. 2–5

The epithelium of the coil appears columnar or cubical according to the degree of distention of the wall; when the lumen is empty the high columnar cells project far into it with their rounded tops which are particularly granular and often contain pigment, especially in the ceruminous glands of the ear. The tops of these cells are abstricted when the secretion is fully matured and pass into the lumen where they liquefy; in preparations fixed in early stages of this process they can be recognized in the lumen, thus demonstrating the apocrine character of the gland. After shedding these processes, which often appear lobed, the cells become lower (cubical) and form on their free surface a distinct cuticular border, in the region of which well-formed terminal bars can be recognized. With renewed activity the cytoplasm becomes obviously granular and the cuticular border disappears as the tops of the cells fill with secretion. Thus the picture presented by these cells varies greatly according to the stage of secretion.

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[1] Occasionally bifurcations appear in the large axillary and circumanal glands.

Outside the secreting epithelium lies the myo-epithelium, a single, interrupted layer of epithelial cells transformed into smooth muscle cells of typical spindle-shaped form lying between the epithelium and the basement membrane. At the boundary of the coil and duct they pass directly into the outer epithelial layer of the latter. They do not rest upon the outer surface of the epithelial layer but are sunken into the bases of the cells.[1] They are by no means in immediate contact but rather lie at short intervals from one another and are distinctly arranged in the form of an extended spiral.

The external layer of the wall of the coil is formed by the basement membrane which in the sweat glands has a very considerable thickness and seems to be of the nature of elastic connective tissue.[2]

Pl. 91, Fig. 4 In the ECCRINE glands the processes of the cell laden with secretion are absent,
Pl. 89, Figs. 1, 2 the cuticular border is indistinct, the lumen is small, and above all the height of the cell — especially in the smaller glands — is slight. Further the myo-epithelial cells are distinct only in the long glands of the palm and sole; in the short eccrine glands the myo-epithelium is either entirely missing or is imperfectly developed and markedly discontinuous.

Pl. 91, Fig. 4 The DUCTS are short and relatively straight in the small eccrine and the large apocrine
Pl. 92, Fig. 6 glands, long and more or less crooked in the long eccrine glands. In the ducts of the latter
Pl. 88, Fig. 3 the part in the corium must be distinguished from that running through the epidermis; the latter part of the duct has no true wall but the cells of the stratum germinativum retreat from one another to form a lumen. In the region of the thick stratum corneum of the palm and sole the lumen winds in a definitely spiral, corkscrew-like fashion.[3] The corial part of the lumen naturally has a true epithelial wall, always of two layers of cells the inner of which represents the direct continuation of the secreting epithelium of the coil. It is cubical and shows indistinctly a cuticular border with terminal bars. The outer layer is a low, cubical epithelium and represents the continuation of the myo-epithelium. Naturally this corial portion also possesses a basal membrane.

The coils of the sweat glands are surrounded by a rich capillary network (p. 299). Non-medullated nerve fibers form a plexus upon the basal membrane and then penetrate it to end between the epithelial cells.

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[1] These grooves appear shallow when the slender ends of the spindle-shaped cells are cut across and deep when the cut part contains the nucleus.

[2] When the lumen of the gland is empty the membrane lies in more or less distinct, ring-like folds which appear in longitudinal sections as indentations of the myo-epithelium. It stains with the dyes used to demonstrate elastic fibers, consequently it is to be considered that elastic fibers share in its formation as well as fibers of reticulum.

[3] However until it reaches the stratum granulosum the intra-epidermal part of the duct has a wall of its own formed of the adjacent cells of the stratum germinativum. From this point onward, particularly in the stratum corneum, the duct is a spiral canal between disintegrating epithelial cells. The sweat carries out with it distinct products of the disintegration of these layers of the epidermis (keratohyalin, eleidin, keratin).

The Mammary Gland, *mamma*

The MAMMARY GLAND is a large cutaneous gland or rather a group of about 12 to 20 Pl. 92, Figs. 9-11 smaller compound tubulo-alveolar glands which, from their embryology and comparative anatomy, are to be considered large apocrine sweat glands. Adipose tissue predominates in the connective tissue which surrounds the individual glands and seemingly combines them into one, so that each separate gland corresponds to a lobe (lobus) of the mammary gland as a whole.[1] Each excretory duct shows an expansion, the *sinus lactiferus*, a short distance from its orifice on the nipple.

During pregnancy the epithelium of the alveoli varies from cubical to columnar according to the stage of secretion and becomes nearly flat when all secretion is discharged. Toward the end of pregnancy the alveolus contains droplets of fat and has a relatively wide lumen.

Secretion in the cells of the mammary gland proceeds according to the type of the apocrine sweat glands,[2] and may very readily be observed because in addition to a fluid secretion containing albumin (casein) there is another with definite form, viz. fat droplets. These first appear in the cell as fine droplets which increase in size and at last are separated from the lumen only by a thin covering of protoplasm. The superficial zone of the cell containing the fat droplets is now abstricted and the latter reach the lumen, each retaining its fine albuminous envelope which prevents the droplets from fusing. Thus during lactation the lumen is often entirely filled with fat droplets. The cells now devoid of secretion regenerate in the same way as those of apocrine sweat glands. The cell when emptied of secretion appears low and usually has a flattened nucleus, for while the fat droplets lay in the protoplasm of the cell they pressed the nucleus against the wall. Beside the fat drops there are also found secretion granules, which are the antecedents of the albuminous constituents of the milk.

Fine, branched, basket cells are found between the epithelium and the basement membrane and doubtless correspond to the myo-epithelial cells of apocrine sweat glands, but have a branched, basket-like (p. 51) form. They are less abundant in the lactating than in the non-lactating gland.

The interstitial connective tissue of the mammary gland is rich in leucocytes and Pl. 92, Fig. 9 eosinophiles. Towards the end of pregnancy leucocytes enter the alveoli of the gland, take from its cells a heavy load of fat droplets and move into the lumen where they bear the name of COLOSTRUM CORPUSCLES. They constitute the formed elements of the colostrum *i. e.* of the secretion of the mammary gland which appears at, and previous to, the time of birth; the formation of true milk does not begin until some days after birth. When the gland is in full activity of secretion following birth the amount of interstitial tissue and leucocytes is considerably diminished. Colostrum corpuscles do not appear again until toward the end of lactation.

The DUCTS of the mammary gland as far as the sinus lactiferus have a low columnar epithelium, occasionally of two layers of cells; in the region of the sinus this passes gradually into the stratified epithelium of the epidermis. A basal membrane separates the epithelium from the connective tissue; there is no musculature.[3]

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[1] See Sobotta-McMurrich, Atlas of Human Anatomy, vol. III.

[2] The mammary gland is derived from such glands.

[3] However in the neighborhood of the opening on the nipple, bundles of smooth muscle surround the duct.

The characteristics of the mammary gland as pictured above are those during lactation. But since the mammary gland, unlike most of the other glands of the body, is only periodically active and as a rule never so in the male sex, there is also an inactive condition whose characteristics are expressed microscopically. During childhood and old age, and in the male sex, the gland consists only of the ducts. In the female sex the alveoli form after the beginning of puberty, but not until pregnancy is there any considerable increase in their number; this increase is at the expense of the interstitial connective tissue which originally was very abundant. The gland does not reach full development until some days after parturition but then remains at this level during lactation. When the latter ceases there begins again an increase of the interstitial connective tissue at the expense of the glandular substance, whose epithelium disintegrates and is removed by phagocytes, until approximately the same condition is reached which existed at the beginning of pregnancy.

MILK, *lac*, consists in the microscopic sense of numerous fine fat droplets averaging 2—5 μ in diameter and of a few scattered cellular elements. The latter, often heavily laden with yellowish fat droplets, form the chief constituent of the colostrum in which free fat droplets are as yet lacking. In the AREOLA of both sexes there are large sebaceous glands, some of which are connected with the fine hairs there present, also well developed sweat glands which form small elevations. During pregnancy many of the large sweat glands develop into accessory mammary glands, the so-called Montgomery's glands. The skin of the nipple and of the areola contains a large amount of smooth muscle and has pigment, usually in considerable quantity, in its epidermis.

The BLOOD VESSELS of the mammary gland form close capillary plexuses around the alveoli. The same relation is shown by the numerous LYMPHATIC VESSELS which begin as blind-ending capillaries in the interlobular tissue. The veins of the areola form a circular plexus and the same is true of the larger lymphatic vessels. The NERVES go partly to the blood vessels and partly to the lobules of the gland where, like those of the salivary glands, they innervate the alveoli. The skin of the nipple and of the areola is rich in sensory nerve endings.

Appendix:

The Microscope and its Use

I. The Microscope

The investigation of the minute structure of human and animal tissues and organs is carried on with the aid of the compound microscope.

A compound microscope consists of objective and ocular (see below), while the simple microscope (magnifier, loupe) has only an objective of low magnifying power. In the latter case the image is seen in the upright position; in the compound microscope the image is reversed.

Microscopes differing in size and equipment but of good quality are supplied by numerous firms; for details the excellent catalogues provided by the manufacturers should be consulted. If it is not possible to purchase at once a complete microscope with homogeneous immersion objective (price about $ 100.00 or £ 20, with elaborate equipment decidedly more) the instrument should at least be capable of subsequent additions which will render it serviceable for all purposes.

A microscope consists of four parts as follows: 1. the TUBE, a cylindrical tube which carries the optical apparatus proper (objective and ocular); 2. the PILLAR, a solid vertical piece of metal which carries 3. the STAGE, and unites the whole instrument with 4. the BASE, a horizontal base of metal usually shaped like a horse-shoe. The pillar is subdivided into a lower part lying beneath the stage and a part above the stage. The latter carries the tube and at the same time bears the devices for focusing the microscope. An exhaustive description of this part, which varies greatly according to the size and construction of the instrument, cannot be given here (see catalogues); however the following points which apply to all instruments should be noted. The PILLAR is massive and is fastened rigidly to the BASE beneath it. Close beneath the stage in medium and large instruments there is a JOINT (knee) by which the entire upper part of the instrument may be bent into a horizontal plane

In most of the recent larger instruments the part bearing the tube begins above this joint. In smaller instruments a circular ILLUMINATING MIRROR, plain upon one side and concave on the other, is fastened to the pillar by moveable joints which permit it to be bent both backward and forward as well as laterally. In large microscopes the mirror is usually combined with the so-called condenser (see below).

The STAGE in the smaller instruments is a horizontal, rectangular plate of blackened metal, or less frequently of hard rubber, which has near its center a circular perforation. In large microscopes it is rigidly connected with the tube carrier. Two CLAMPS inserted into small holes near the hinder corners of the stage serve to hold the preparations. Large microscopes usually have a circular stage consisting of a lower, rigid plate and an upper plate which may be moved and centered by screws.[1] On the under surface of the stage of small microscopes there is a diaphragm, now usually of the iris type.[2]

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[1] Large instruments are often provided with a stage which may be moved by screws in two directions perpendicular to one another; scales for reading the position are also provided. Usually such stages are also made to revolve.

[2] Disc and simple cylinder diaphragms are now rarely used.

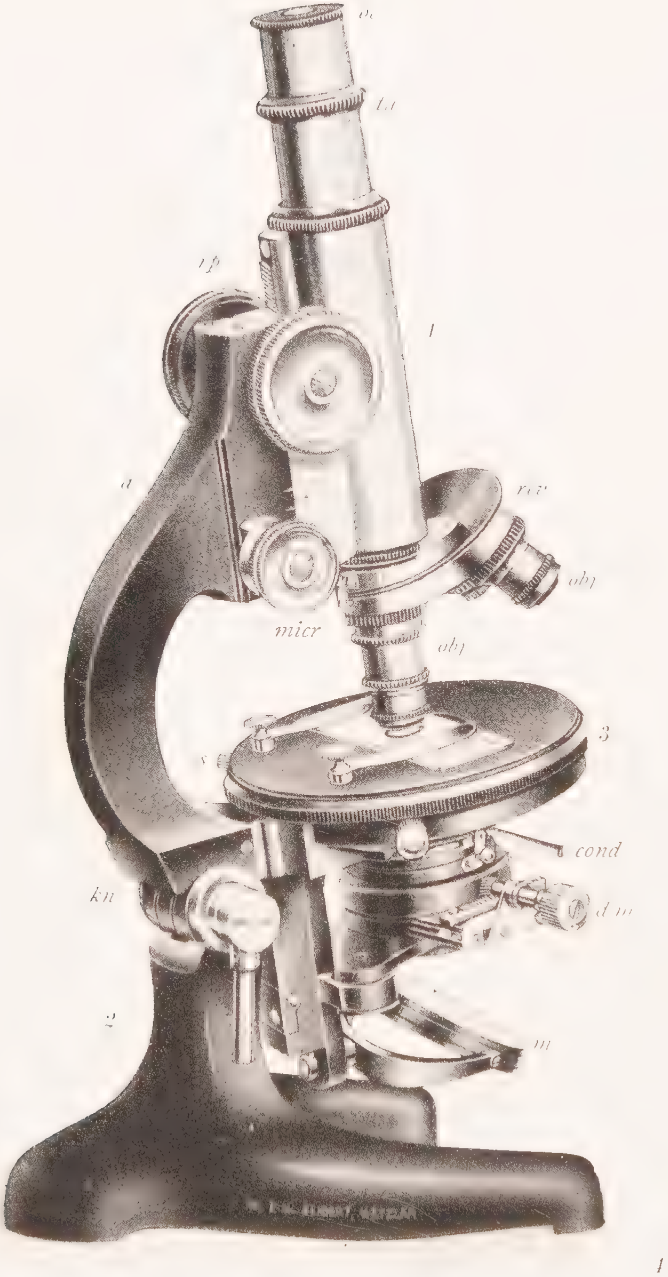

Fig. 38. **A Mediumly Large Microscope.**

W. & H. Seibert, Wetzlar

(About $^1/_2$ actual size)

Draw-tube with scale, revolving nosepiece, condenser, round stage with screws for centering.

1 = tube
2 pillar
3 = stage
4 = base

a = arm
cond = condenser
d m = mounting of diaphragm
kn = knee and clamp
m — mirror
micr = micrometer screw
obj = objective
oc = ocular
rev = revolving nosepiece
r p = rack and pinion
s = screw for centering stage
tu – draw-tube

In place of the cylinder diaphragm all large microscopes are provided with an ABBÉ ILLUMINATING APPARATUS or CONDENSER, a system constructed of two, or more often of three, thick glass lenses of short focus and so adjusted as to concentrate the light from the mirror upon a point immediately above the stage of the microscope. The condenser in its cylindrical metal mounting is either inserted in a well-fitting sleeve or, as is the case with all the larger instruments, the entire mechanism which serves to illuminate the microscopic preparation (*i. e.* condenser, iris diaphragm and mirror) is attached to the tube carrier by means of a vertical metal piece provided with a rack and pinion. The illuminating mechanism thus follows the movement of the microscope when it is bent at the joint mentioned above. The rack and pinion serves to raise and lower the condenser. Beneath the condensor is an IRIS DIAPHRAGM in a mounting which is moveable laterally, thus rendering it possible to obtain oblique illumination through an opening of any desired size.

To obtain the so-called DARK-FIELD which is of advantage in many investigations in normal histology, the ordinary condenser is replaced by a (paraboloid) dark-field condenser, or a condenser is used which can provide for both ordinary and dark-field illumination.

More important than the parts just described, which lie beneath the stage, are the UPPER PARTS of the microscope. All microscopes of medium and large size, and recently the smaller microscopes as well, have at the back of the tube a RACK AND PINION by which the tube may be moved for purposes of focusing.[1] In addition the arm of all microscopes has a so-called MICROMETER SCREW for "fine adjustment" of the focus. This is accomplished either by a screw-head placed at the upper end of the arm, or in smaller instruments at the upper end of the pillar. Or beneath the pinion screws there may be found two small graduated[2] cylindrical screws or DRUMS for controlling the fine adjustment. This control in older instruments was obtained by a screw at the upper end of the pillar but in later types by two small drums, right and left.

The TUBE of all medium and large microscopes is double, that is, within a slightly wider outer tube there is inserted a narrower tube which slides in and out and is marked by a scale. The length of the tube as a whole may thus be varied from time to time and is indicated by the reading on the scale. The lower, somewhat conical, narrowed end of the tube is threaded for the reception of the objective, while the upper, open end of the inner tube receives the ocular. Small instruments have a tube of fixed length (170 mm.).

OBJECTIVE and OCULAR alone represent the optical apparatus of the microscope and produce the microscopic picture. All other parts of the microscope are accessories and form the so-called STAND of the microscope.

The OBJECTIVE is a system of lenses, the separate lenses being firmly incorporated in a cylindrical or conical metal mounting.[3] The lower lens, next to the microscopic object is known as the FRONT LENS and is at once visible when the objective is viewed from without. At the opposite end of the objective is the thread by which it is fastened into the lower end of the tube. The size of the front lens indicates whether the objective is of low or of high magnifying power. The smaller the front lens the greater the magnification given by the objective as a result of its shorter focal distance.[4]

Objectives, particularly the so-called apochromatic objectives, give an enlarged picture of the object in true color, but one which is reversed in position by the use of the ocular. Objectives are designated either by selected letters or numbers, in which case the first number (I. 1) or letter (A. a) indicates the lowest magnification; or they bear as designition, the focal length in millimeters *e. g.* apochromatics 16 mm., 8 mm., 2 mm. etc.[1] According to its focal length the objective gives an INITIAL magnification of about 3—125 diameters. A distinction is made between DRY SYSTEMS and IMMERSION SYSTEMS. In the former a layer of air remains between the front lens of the objective and the cover-glass of the microscopic preparation. In the immersion lenses this space is filled either by water (water immersion) or oil of cedarwood (oil or homogeneous immersion). Immersion lenses, (those commonly employed are of the homogeneous immersion type) are objectives of short focal length and consequently of high magnifying power, in which air of low refractive index is replaced by the cedarwood oil of high refractive index in order to attain a higher NUMERICAL APERTURE for the objective.

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[1] The old type of instrument in which the coarse focusing was accomplished by movement of the tube within a lined sheath is now scarcely ever used.

[2] The movement through one degree of these micrometer screws signifies a raising or lowering of 0.001—0.002 mm. according to type of construction and make; while the rotation through one degree of the similarly marked screw at the upper end of the pillar in the old form of micrometer means a movement of 0.01 mm. The newer adjustment, which is constructed by different firms according to different principles, is thus far more delicate than the old.

[3] Not all objectives have a mounting which cannot be varied. In order to admit of correction according to the thickness of the cover-glass of the microscopic preparation "dry" objectives of high power are so constructed that the lower lens system (front lens) may be moved in relation to the upper. The objective carries a scale upon which necessary changes in position may be read for each thickness of cover-glass between 0.1 and 0.2 mm. (so-called correction collar: Fig. 41). In other objectives of weaker magnification a similar mounting serves to alter the magnifying power of the objective itself.

[4] In dry systems the same may usually be recognized by the lengths of the various mountings.

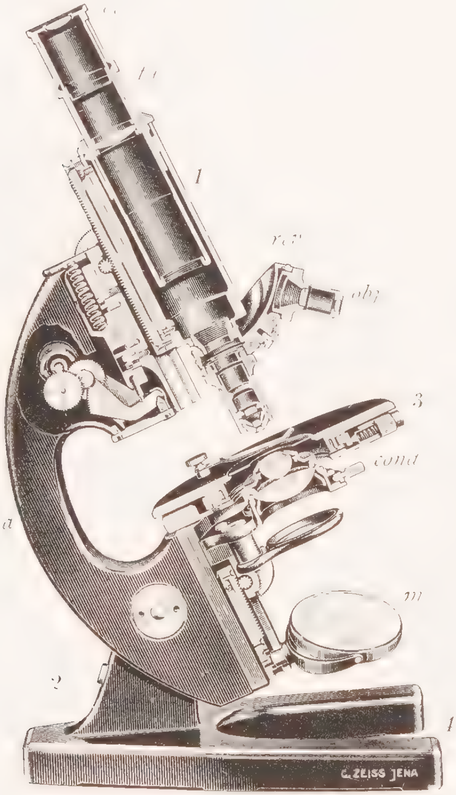

Fig. 39. **A Longitudinal Section of a Large Microscope.**

C. ZEISS-JENA

(about $^1/_3$ actual size)

The arm differs somewhat in construction from that of Fig. 38

References as for Fig. 38.

The resolving power of an objective, particularly one of high magnifying power, depends not merely on the focal length of its lenses, the magnifying power of which is not extreme, but primarily upon the numerical aperture (a). This quantity is the product of the refractive index (n) of the medium (air, water, oil) which intervenes between the object and the objective, and the sine of half the angle through which light enters the objective, (u); ($a = n \times \sin u$). Since the refractive index of air is 1. no dry system can attain an aperture of 1.0 but is always less; for sin u must always be less than 1. The use of cedar oil which has a refractive index 1.52, permits an aperture of 1.40 to be obtained in favorable cases. Such a lens, although it may have the same focal distance as a lens of less aperture, *e. g.* 1.30, has much the greater power of resolving microscopic structure. Indeed a homogeneous immersion objective of 3 mm. focal length and 1.40 aperture has a better resolving power than one of 2 mm. focal length but only 1.30 aperture; or in other words it is useless to increase the magnification unless the aperture is adequate.

The OCULAR is a much simpler component of the microscope. Simple oculars (Huyghenian) consist essentially of a combination of two lenses in a cylindrical mounting the upper end of which has a border projecting beyond the upper edge of the tube to prevent the ocular sliding down into the latter. The upper lens of the ocular is named the EYE LENS the lower the FIELD LENS. The former is plano-convex with the plane surface towards the observer; the latter is either plano-convex or bi-convex. Between the lenses and in the interior of the ocular, which usually is short, a fixed DIAPHRAGM is so placed that the real picture formed by objective and field lens falls in the plane of the diaphragm. Oculars are usually designated by an arbitrary selection of figures; thus the HUYGHENIAN oculars commonly used, are marked 0, 1, 2, etc. or 0, I, II, etc. in which 0 or 1 (I) indicates the ocular of least and 4 (IV) that of greatest magnifying power. Or else the figures are selected, as in the case of COMPENSATION oculars, and recently of others, so that the number corresponds to the initial magnification of the ocular. Besides having an eye lens of smaller diameter (shorter focal length) oculars of higher magnifying power may be distinguished from those of lower magnifying power by being shorter.[1] In use the ocular rests in the upper end of the microscope tube, from which it may at any time be lifted out and replaced by another ocular.

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[1] The non-apochromatic homogeneous immersion lenses of most firms are still usually designated by their approximate focal length expressed as a fraction of an inch ($^1/_{12}$, $^1/_{16}$). As a matter of principle each objective should be named only by its focal distance in millimeters.

Most studies with the microscope require the use of three objectives of different focal length and therefore of different magnifying power. Consequently microscopes of large, and usually those of medium size, are provided with a device known as a REVOLVING NOSEPIECE for changing the objectives. This device consists of a perforated plate which screws into the lower end of the tube and carries a revolving disc with three to five openings[2] for the reception of the objectives. As the lower disc revolves each opening is brought in turn[3] beneath the lower end of the tube. A click given by a spring indicates when an opening in the disc coincides with the opening at the end of the tube.

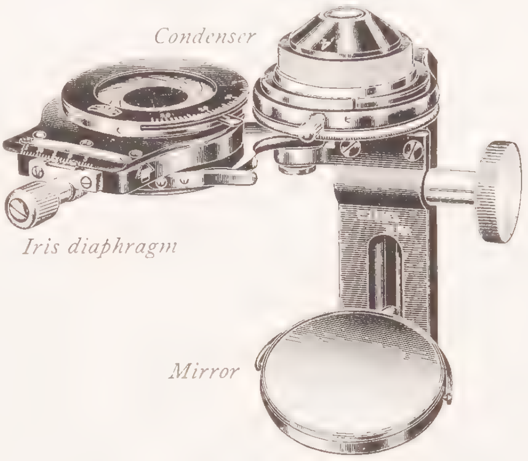

Fig. 40. **The Illuminating Mechanism of the Microscope. Condenser, Iris Diaphragm, and Mirror**

C. ZEISS-JENA

The iris diaphragm has been swung out to the left

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[1] One should not be deceived by the length of certain types of ocular *e. g.* the stronger compensation oculars (8, 12, 18). The lenses of these oculars are placed quite close together and the remainder of the mounting is empty. These oculars are not simple lenses, but are specially corrected systems. The same is true of the complanation oculars (also known as orthoscopic or periscopic oculars) which aim at flattening the microscope field and have the upper surface of the eye lens convex, not flat. Such oculars are much more expensive than the more simple Huyghenian oculars which can only give a field that is considerably curved.

[2] A revolving nosepiece for only two objectives is not advisable since it greatly restricts the number of lenses that may be used. At the same time nosepieces for five objectives are not greatly to be recommended, those for three or at most four objectives are to be preferred. Microscopes without rack and pinion, in which coarse focusing is obtained by moving the tube within its sleeve, are not adapted for use with a nosepiece.

[3] For delicate work such as microphotography sliding nosepieces are used in place of the revolving nosepiece. These are superior to the revolving nosepiece because, in the first place, any desired number of objectives may be interchanged, secondly because the objectives can be exactly centered, a thing which unfortunately can never be done exactly with a revolving nosepiece. However the use of the sliding type is rather less handy than that of the revolving nosepiece.

For ordinary studies in human histology and microscopic anatomy dry lenses are used, rarely immersion lenses[1] the manipulation of which is more difficult for a beginner. THREE dry lenses, of which one has a very low magnifying power[2] form a better selection than two lenses. The LOWEST in magnifying power should be of about 20—30 mm. focus, the NEXT, 8—12 mm. focus and the HIGHEST 3—4 mm. focus. A homogeneous IMMERSION lens may easily be procured later. Usually an achromatic immersion $^{1}/_{12}$ is used. The very expensive apochromatic immersion lenses have indeed great advantages over the achromatic lenses, but their full superiority appears only if very strong oculars are employed. In their place fluorite lenses are to be recommended as superior to the ordinary achromatic immersion objectives. The stronger fluorite dry lenses also give better results than the ordinary achromatic systems.

ORDINARY HUYGHENIAN oculars are as a rule employed with the achromatic objectives commonly used. Two of these are sufficient, one of low power (no. 0 or 1) and one of medium power (no. 2 or 3). Large instruments usually have three or more. These oculars have the fault of not giving a flat field; consequently the micrometer screw must be used constantly to attain a sharp picture from both center and periphery of the field. Where, as in projection, etc. this is inadvisable complanation oculars[3] are used. Apochromatic lenses and to some extent fluorite lenses require special oculars, so-called COMPENSATION oculars (see above). Here a large number of oculars (usually five or six) is an advantage because apochromatic objectives permit the employment of oculars of comparatively high magnifying power. For such objectives only compensation oculars should be employed.

The MAGNIFYING POWER of a microscope is obtained from the initial magnifications of objective and ocular, and is easily determined if the focal length of the objective and the initial magnification of the ocular are known. Frequently these are given on the mountings, otherwise tables of magnification etc. may be consulted in the catalogues.[4] To obtain the magnification of combined objective and ocular the quotient of the image distance (250 mm.) divided by the focal length of the objective is multiplied by the initial magnification of the ocular. For example, an objective of 2 mm. focal length has an initial magnification of 125 diameters (250—2); with a 2 × ocular the total magnification of the microscope will be 250 ×; with 4 × ocular, 500 ×; with 8 × ocular, 1000 ×; with 12 × ocular, 1500 ×; etc. It is taken for granted in this that the length of the tube is (160 —) 170 mm.[5]

A truly sharp and correct picture can only be produced by a definite TUBE LENGTH and a definite THICKNESS OF COVER-GLASS. Most firms, consequently, adjust their objectives to a tube length of 160 (—170) mm. and a cover-glass thickness of 0.17 mm. (0.16 – 0.18 mm.). With dry systems of low and medium power and also with homogenous immersion lenses VARIATION IN THE THICKNESS OF COVER-GLASSES is a matter of little consequence. In the first case, because the distance of the front lens from the object is large and the intervening air space has a considerable length; in the second case because immersion oil has about the same refractive index as glass.[1] But an alteration in the thickness of the cover-glass injures the picture in the case of dry systems of high magnifying power because the front lens is separated from the surface of the cover-glass by only a very thin layer of air (see below). On this account it is of advantage that such objectives should permit of correction for cover-glass thickness by rotation of the scale on the correction collar in reference to the mark on the other portion of the mounting. The objective may be adjusted to cover-glasses of a thickness of 0.1—0.2 mm.[2] As a result it is an advantage always to use cover-glasses of definite and known (0.16 mm.) thickness. If preparations are mounted only with cover-glasses of this thickness the correction collar would be superfluous; but since this, unfortunately, is not usually the case the fault of the cover-glass must be corrected. This may be done using the scale as described above, if the thickness of the cover-glasses employed has previously been measured. Or it may be done by trial, the correction collar being rotated in one direction or the other until perfect sharpness of the picture is obtained.

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[1] Oil immersion lenses are understood; water immersion lenses are used only for very special purposes such as examination in water without a cover-glass.

[2] Instead of a very weak objective, in case of need a good pocket lens (aplanatic loupe) may be used, or even an ocular, the eye lens of the latter being applied to the preparation.

[3] As to complanation oculars see p. 315 footnote 1.

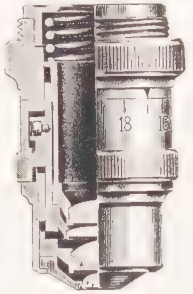
[4] If a revolving or sliding nose piece is used its height must be reckoned as part of the tube length; thus the latter should be set at about 155 mm.

[5] The magnifications as given in catalogues are usually average values and cannot be relied upon. Consequently verification of a table of magnifications is necessary.

Fig. 41. **Objective** (dry, high power) **with Correction Collar for Cover-Glasses of Different Thicknesses.** (C. Zeiss-Jena)

The numbers on the moveable collar indicate the cover-glass thickness in hundredths of a millimeter

Note that all the lenses are confined to the lower part of the mount.



If there is available no dry system of high magnifying power which is provided with a correction collar (and such a collar increases the cost of the objective very considerably) a certain amount of adjustment may be obtained by changing the tube length. For cover-glasses thicker than 0.17 mm. a certain degree of correction may be obtained by shortening the tube to 150—160 mm. For thin cover-glasses the length of the tube must be increased to 180 or even 190 mm.

CHANGING THE TUBE LENGTH used with dry systems of low and medium power is without appreciable influence on the excellence of the picture. Lengthening the tube will produce an increase in the size of the microscopic picture without harm to the definition. The longer the tube the larger the picture because the diverging rays of the objective are received by the field lens of the ocular at a greater distance. (see the diagram of the path of the rays *Fig. 42*). With high magnifications the case is otherwise. Here the excellence of the picture suffers very considerably from the change in the tube length. In particular IT IS A GRAVE MISTAKE IN PRINCIPLE TO WORK WITH HIGH MAGNIFYING POWER AND EXCESSIVE TUBE LENGTH; however this mistake is commonly made. A moderate elongation of the tube would be permissible only on the supposition that the cover-glass is extremely thin, and such is not likely to be the case. The physical optics of the microscope will not be treated here. The accompanying picture illustrates the path of the rays.

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[1] Naturally it is pretty much the same whether the interval between objective and object is filled mostly by glass or by oil, but a cover-glass which is too thick often prevents the use of an immersion lens since the latter, because of its short focal length, has only a very small free working distance. A yet greater disadvantage is an oblique cover-glass *i. e.* a cover-glass which rests upon a layer of Canada balsam of unequal thickness (see footnote 2).

[2] Too thick a layer of Canada balsam between preparation and cover-glass has the same effect as a cover-glass of too great thickness. Indeed such a layer may render impossible the examination of a preparation with an immersion lens.

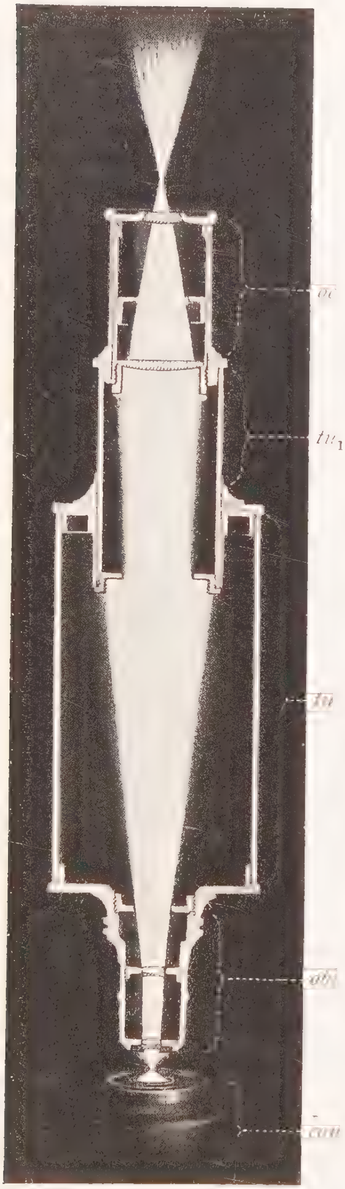

Fig. 42. **The Path of the Rays through the Microscope.**
(Emil Busch, A.-G., Rathenow)

con = condenser
oc = ocular
obj = objective
tu = fixed tube
tu_1 = draw tube

II. The Use of the Microscope

In the use of the microscope, which with the beginner is often one of the smaller instruments, the following points are to be noted. The microscope is taken from its case, locker, etc. and placed with the illuminating mirror towards the source of light (daylight or artificial light). In older instruments the tube is drawn out of its sheath and light is directed through the latter by the mirror of the microscope. To determine this, the opening in the stage of the microscope is covered by a piece of translucent paper and the mirror is turned so that the paper is well illuminated. The paper is then removed and replaced by the preparation without disturbing the microscope. The objective and ocular are next fitted in the tube, the tube being rotated and thus screwed to the objective, not vice versa, then the tube is replaced in the sheath by a careful rotating movement until the picture of the preparation becomes almost sharp. The final focusing is done with the aid of the micrometer screw.

To-day, however, a stand with rack and pinion for coarse adjustment is usually available and as a rule a revolving nosepiece also. The latter is fitted with two or three dry systems following one another clockwise, in increasing strength of magnifying power.[1] Light is obtained in the manner described above, using an opening in the nosepiece in which an objective has not been fitted. However the source of the light is readily located through the weakest objective on the nosepiece. Coarse focusing is accomplished by the rack and pinion and the exact focus abtained by the micrometer screw.

Examination is made first with low magnifying powers and gradually increased by use of objectives, and perhaps also of oculars,[2] of greater magnifying power. With a very low magnification the PLANE MIRROR must be used, while with medium and high magnification as a rule the CONCAVE MIRROR is employed.[3] The Abbé illuminating apparatus (condenser) and the plane mirror should be used for high magnification. This is ESSENTIAL in obtaining the full efficiency of the condenser and this in turn is absolutely necessary when immersion lenses are employed. It is better to use the concave mirror with dry systems of medium power if the condenser is to be used instead of exchanging the latter for a cylinder or other diaphragm, a thing which often is inconvenient.[1]

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[1] If an immersion lens is to be employed the weakest dry system is to be removed, for in such a case it can usually be dispensed with and replaced by the immersion lens, which then falls into its proper place. The use of a quadruple revolving nosepiece is better and more convenient.

[2] In contrast to apochromatic systems, the achromatic dry systems of high magnifying power will work well, as a rule, only with oculars of medium power (see below).

[3] If unstained objects are being examined or structures that are very delicate and pale, the plane mirror is often the better with medium and even with high magnifications.

In CHANGING THE OBJECTIVES of old models of small microscopes without revolving nosepiece (such as now are rarely used) the tube must be withdrawn from the sleeve. The palm of the hand is placed over the ocular so that the latter may not fall out, the objective previously in use is unscrewed and replaced by the new objective and the tube is reinserted in its sleeve. Oculars may be changed while the tube is in place. In microscopes with revolving nosepieces, the objectives are changed by rotating the nosepiece which has been fitted with objectives previous to using the microscope. As a rule the mounting of the objectives is such that lenses of great magnifying power have longer mounts than those of lesser power. Consequently in passing from one magnification to another it is not usually necessary to make use of the coarse rack and pinion adjustment.[2]

The use of the more powerful objectives, either dry or immersion, requires special care. As a rule these have a very short working distance and must be advanced to within a fraction of a millimeter from the microscopic object or its cover-glass. This must be done with great caution, otherwise the cover-glass may easily be broken or the preparation rendered valueless merely by pressure on the cover-glass. There is also the danger of injury to the expensive lens, particularly of loosening the front lens of an immersion objective of high power. To avoid these mishaps the object is placed exactly in the center of the field of a weak objective before the stronger objective is brought into use. Then, provided the centering of the lenses and the nosepiece is moderately exact, careful lowering of the tube is sure to bring the object into the field of the stronger objective. In using an immersion objective a drop of immersion oil must be placed upon the cover-glass; then the tube is lowered until the front lens of the objective touches the oil. This movement is controlled FROM WITHOUT by looking at the instrument from the side. After making sure that contact has been made with the oil, the focusing is completed as usual by observation through the ocular. Care must be taken that the oil contains no air bubbles; these are very troublesome. In passing from immersion objectives to dry systems of high power the oil must be removed from the cover-glass, preferably by the use of ether. If examination is to be made with weak lenses and for a short time only, the presence of the oil causes little trouble. After using an immersion objective its front lens must be carefully cleansed of oil, best by means of a piece of chamois skin moistened with ether.[3] Work with immersion objectives thus demands special care.

In employing objectives of medium and high power the DIAPHRAGM should never be forgotten since delicate structural features are often lost through the use of too wide an opening. The iris diaphragm, which is always provided on medium and large instruments and usually on smaller ones as well, affords any desired degree of illumination, the optimum being easily determined by trial. However there are cases in which it is of advantage to work with the full illumination given by the condenser, for instance, when rapid search is being made for small but strongly stained objects such as bacteria. In this case the brilliant illumination makes very pale the background, which is stained little if any, while the objects stained come the more distinctly into view. These considerations are most frequently of advantage when homogeneous immersion lenses are employed. For purely histological examination they are of minor importance. Examination with a homogeneous immersion lens always demands the use of a condenser (see above).

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[1] If the condenser is to be retained with the use of the very weak dry systems, it may advantageously be lowered until the interference by the pictures which it forms (window bars etc.) has disappeared. In recent instruments a condenser which swings out of the way is commonly provided. On the upper surface of its mounting there is a convex iris diaphragm.

[2] This observation on the length of objectives is not absolutely exact. In particular it is not true for very weak objectives which, at the same time, are short. In the sliding type of nosepiece (p. 315, footnote 3) the correction is such that the various objectives come exactly into focus when they are exchanged. Immersion objectives are not made thus to fit, since in passing to them from dry systems oil must first be inserted.

[3] A special grade of soft paper — lens paper — may be obtained from the manufacturers of microscopes and is to be preferred to chamois. The stock should be kept free from dust and a piece once used should not be used a second time. — Trans. note.

It must always be realized that the best and most useful magnification is obtained essentially by the objective; that the ocular of itself can only re-magnify the picture afforded by the objective and in so doing all the faults of the picture will also be magnified. As a rule the correction of the optical defects inherent in glass lenses (spherical, and chromatic aberration) is accomplished by the use of different kinds of glass in the OBJECTIVE. The ordinary (Huyghenian) oculars are composed of two simple lenses of ordinary glass and cannot improve the microscopic picture. Indeed on the contrary, they increase the defects of the picture given by achromatic objectives. The matter is somewhat different in the case of apochromatic objectives which derive their name from their superior correction of chromatic aberration. Here the use of compensation oculars does, in a certain sense, improve the picture for they share in doing away with the chromatic aberration.[1] From this it is evident that only apochromatic objectives should be used with this type of ocular. The pictures so produced show no marginal colors in contrast to a slight, but scarcely injurious, band of color in the margin of the circular field of view of achromatic objectives. As a result with apochromatic objectives a more powerful ocular may be used than the ordinary uncompensated ocular such as is commonly found in use with achromatic objectives. However even with apochromatic objectives the more powerful oculars do not improve the picture. Indeed if it is a question of sharpness of delineation they are even detrimental. Naturally the same is true in a much higher degree in the case of achromatic lenses and the ordinary Huyghenian oculars of great magnifying power.

Conditions are such that in practice it is most advantageous to make examinations with the aid of oculars of medium strength. Oculars of low magnifying power (3—4 times) are termed "searching oculars" because they give large fields of view in which a considerable portion of the preparation may be surveyed in order to locate the part to be examined in greater detail. In itself the magnification obtained by a searching ocular is too small for the study of microscopic preparations. This is done best with the aid of oculars magnifying from seven to ten times. Oculars which magnify more than tenfold in general do not give a useful magnification, this is particularly the case when they are used with achromatic objectives. But with apochromatic objectives much higher powers, up to fifteenfold, are of advantage. Naturally the focal length of the objective enters into the question; the less the objective magnifies, the more the microscopic picture may be magnified by the ocular without appreciable harm. The greater the initial magnification of the objective, the more caution must be used in employing oculars of high power.

In the use of the microscope the correct method of employing the MECHANISM FOR EXACT FOCUSING (micrometer movement) is of the greatest moment. The sharpness of focus obtained by the aid of the rack and pinion is sufficient for examination under low magnification only. When magnification above medium strength is used, and more particularly in the case of high magnification, precise focusing must be obtained by the use of the micrometer screw. Unlike the screw for coarse focusing the latter is not released from the hand when a sharp focus is obtained but THE HAND (this may be either hand in the case of modern instruments which bear screws of like action on both sides of the arm) REMAINS ON THE SCREW DURING THE WHOLE PERIOD OF MICROSCOPIC EXAMINATION and treats it so to speak, like the steering-wheel of an automobile. "Backlash" in a fine adjustment is a fundamental fault, for the higher the magnification the more shallow does the optical plane become; *i. e.* the depth of the plane within which an object is sharply pictured. Most preparations which are examined are decidedly thicker than the optical plane, consequently if the limits of sharp vision are not continually altered by means of the fine adjustment only a portion of the thickness of the preparation will be seen. The parts lying in other optical planes would escape completely were the micrometer screw not used, and used continuously, in order to combine the parts of the field which lie in different optical planes.[1]

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[1] Apochromatics are over-corrected in regard to blue, a fault which is re-corrected by the compensation oculars.

For the **care** OF THE MICROSCOPE the following rules may be given. Solidly constructed as are the microscope stands of all the better firms, they must nevertheless be handled considerately and with expert care. Instruments of older construction which carry the older type of micrometer movement at the upper end of the pillar are best grasped by the base. All the newer instruments are so constructed that they may be seized by the arm without injury. The arm is either shaped for gripping or has a handle. It has already been mentioned that the microscope must be guarded from dust by the use of a case, locker, etc. Dusty or dirty stands are best cleaned dry or by water. Alcohol dissolves the lacquer. The exposed surfaces of the lens (the eye lens of the ocular, front lens of the objective, upper surface of the lens of the condenser) are to be wiped off with a soft piece of chamois skin. If they are soiled *e. g.* by immersion oil or Canada balsam, the chamois is moistened with ether or xylol and the deposit dissolved, but carefully, without wetting the metal mount. Never take the objective apart. If it is very dirty, send it to the maker for cleaning. Oculars may be taken apart for the purpose of cleaning should the inner surfaces of the lenses become dirty. Dirt in the ocular may be recognized by seeing it move with the ocular when the latter is rotated in the tube. The two lenses of the ocular (eye and field lenses) are never removed together lest they be replaced in the wrong ends of the cylinder; in which case the diaphragm within the ocular is no longer in the proper plane. Special care must be taken of the micrometer screw. It should always occupy a position midway in its excursion. Frequently marks are made on the tube-carrier indicating the lowest and highest positions of its movement. If it overruns its course it should be replaced immediately. The stand of the microscope should never be taken apart. From time to time it should be returned to the maker for oiling etc.

The microscope may be used in a perpendicular position or, if provided with a joint, it may be inclined. The latter position is particularly to be recommended for high stands if circumstances, such as examination in a fluid medium, do not prevent. Usually illumination in this position is also more convenient. Many instruments have a clamp for fixing the joint in any desired position.

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[1] Using the microscope without keeping the hand on the micrometer screw is a frequent fault of beginners who are apt to urge that they already see a sharp picture. They only do so in the case of low magnifications and very thin sections.

The ILLUMINATION of the microscope and the source of light are of great importance. Although daylight is very good yet it has its disadvantages.[1] Direct sunlight is not to be used because of danger of blinding the retina, neither does the blue light of the sky serve as a good light for the microscope. The best light is that reflected from a white, sunlit cloud or from a light colored wall. But since the conditions and time of day vary so greatly, recourse must be had to artificial light of such quality that it may perfectly replace daylight. Nowadays electric light is almost universally available; for almost all purposes an opalescent bulb of sufficient candle power (about 40—50) is sufficient. It gives a clear but diffuse light that is inferior to daylight only in being deficient in blue rays. In case this is markedly disadvantageous it may readily be compensated by placing in the diaphragm a blue glass which, in different shades, is provided with almost all instruments.

Nevertheless the use of a special microscope lamp is to be recommended for many purposes such as dark-field illumination (see below). Such lamps, in different designs, are supplied by many firms whose catalogues should be consulted.

So far only the use of microscopes of ordinary form has been considered, such as produce a reversed monocular picture. For many purposes a microscope which permits BINOCULAR VISION is to be recommended, the advantage over the monocular microscope being that the picture acquires depth. Particularly when thick layers are to be examined, *e. g.* several layers of blood vessels or nerve plexuses lying one upon the other, there is a great advantage in binocular vision. This is attained by the aid of a special binocular or stereoscopic microscope which carries paired objectives and oculars that match perfectly. The latter are set at an angle to one another in drumlike tubes which contain prisms and which are adjustable to the interpupillary distance. But such microscopes afford only a moderate magnification (up to 100 diameters). Recently in place of a binocular microscope fitted with pairs of matched objectives, a binocular tube is used or a binocular attachment which will set in the single tube. In this manner observations may be made with a single objective but with doubled oculars; thus a stereoscopic effect is produced, which although it may not be strong, can be obtained with the highest magnifications. The most modern instruments are provided with interchangeable single and binocular tubes. Working with a binocular microscope has the further advantage of not tiring the eyes to anything like the same degree as occurs in monocular observation.

Another type of examination with the microscope which is more and more frequently in use is the so-called DARK-FIELD examination. In this case the contours of the objects under investigation are sharply illuminated against a dark background, *i. e.* the field of view is dark, not bright as in ordinary usage. The objects thus stand out much more sharply than in "bright-field" examination. This result is obtained by the aid of a special (paraboloid) condenser which replaces the ordinary condenser. Frequently the so-called "dark-bright" condenser is used which permits immediate change from the one manner of illumination to the other.[2]

For many histological investigations examination by means of POLARIZED LIGHT, obtained by the aid of a polarization microscope, is important. Any microscope with a revolving stage may be converted into a ,,polarization microscope" by the use of a special polarization condenser on the one hand and on the other hand of an analyser which rests on the ocular.[3]

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[1] Occasionally artificial light is a necessity *e. g.* in dark-field examinations (see below).

[2] For details see catalogues and directions for the use of dark-field illumination.

[3] Examination by polarized light, so important for many purposes, demands an exact knowledge of the mode of action of the auxiliary instruments above named. Further details cannot be given here.

While ordinary transparent objects may be examined by transmitted light as has been previously described, it is also possible to examine opaque objects microscopically. Naturally this can only be done by REFLECTED light but recently the limits within which this is possible have been considerably extended. If it is a question of very low magnification it is sufficient to dispense with the microscope mirror and to illuminate the object under examination by any sufficiently bright light, possibly with the aid of a convex lens. Frequently for such purposes instead of the compound microscope the employment of a simple microscope (p. 311) is to be recommended. The latter may be either a mounted loupe or a binocular magnifier (see catalogues).

Should somewhat higher magnification be needed in conjunction with reflected light, the simple arrangements described above are not serviceable because the objective must be placed much too close to the object. In this case special auxiliary instruments are required, such as commonly are used for low magnifications in histological-embryological investigations; namely a concave mirror (so-called Lieberkühn's mirror) attached to the objective. For still higher magnifications, in place of this possibly the so-called vertical illuminator[1] may be required, the use of which can scarcely be discussed here.

III. The Measurement and Drawing of Microscopic Objects

The MEASUREMENT of microscopic objects is accomplished with the aid of an OCULAR MICROMETER. This is a thin glass plate provided with a scale usually of 5—10 mm. each of which is divided into ten or twenty parts. After removing the eyelens this glass, which usually is round, is laid on the diaphram of the ocular. When the eye lens is replaced a sharp picture of the scale[2] lies across the field of view. However the value of each degree is not known, moreover the value changes with the focal distance of the objective employed and must be determined for each objective.

The higher the magnification the less becomes the value of each degree of the micrometer. The value of a degree consequently must be determined with the aid of an OBJECTIVE MICROMETER. This should be done for each instrument and no reliance placed upon the tables frequently supplied with the microscope. An OBJECTIVE MICROMETER consists of an ordinary glass slide which bears an extremely finely divided scale (1 mm. divided into one hundred parts). The position of the scale is usually indicated by concentric rings in order that it may be the more easily found. The microscope is focused upon the scale, a procedure which is rather difficult and requires a narrow diaphragm. The ocular micrometer is placed in the ocular and the two scales made to lie one exactly over the other. It is then easy to determine how many degrees of the objective micrometer correspond to one interval of the ocular micrometer. Since one degree of the former measures 10 μ, one degree of the ocular micrometer will also measure 10 μ if it coincides with a degree of the objective micrometer. If an interval of the ocular micrometer covers four degrees of the objective micrometer, its value is 40 μ. However should four intervals of the ocular micrometer correspond to one of the objective micrometer then the value of each interval is 2.5 μ. ($4 \times 2.5\,\mu = 10\,\mu$). The former will be the case with medium magnifications and the latter with high magnifications. A value of 40 μ for one degree of the ocular micrometer will be obtained with very low magnifications only.

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[1] Commonly this is used only in mineralogical investigations.

[2] In special, so-called measuring, oculars the eyelens is in a separate mounting, by rotating which the scale may be brought sharply into focus. But as a rule all oculars give a sufficiently sharp picture of the scale. The engraved surface of the ocular micrometer is to be laid downward upon the diaphragm.

The objective micrometer also serves for the determination of the MAGNIFYING POWER OF AN OBJECTIVE. By the aid of a drawing apparatus (see below) the scale is projected upon a horizontal sheet of paper and traced. The distance between two graduations, which on the objective micrometer is 10 μ, is then measured with an accurate rule. From the amount of enlargement which one degree (10 μ) has undergone it is possible to calculate the magnification; *e. g.* if the distance between the two graduations on the tracing is 4 mm. the magnification is 400 diameters.

The DRAWING of microscopic objects is usually accomplished with the aid of special apparatus, named on this account a DRAWING APPARATUS. However it is possible to copy microscopic objects by looking through the microscope with the left eye while sketching the picture free-hand on a sheet of paper laid close to the microscope. The right eye controls the sketching. Accurate drawings can be made only with the aid of a proper drawing apparatus. Concerning the numerous types of these, information may best be obtained from catalogues of manufacturers. According to their structure and manner of use there are two distinct types of drawing apparatus: 1. those by which the microscopic picture is projected upon the drawing surface, so-called, projection drawing apparatus; 2. those in which there is obtained a subjective blending of the microscopic picture and the drawing surface. This is usually accomplished by the aid of prisms and mirrors.

In the first case the real picture is projected upon the paper and traced without looking through the microscope. In the second case the apparatus is attached to the ocular and the microscope is used in the ordinary manner. The picture of the pencil as it makes the drawing is thrown into the microscope and combined with the ordinary microscopic picture. Although excellent results may be obtained by both methods it is unquestionably much more simple, certain and easy to work with the projection of the figure on the drawing surface. Quite possibly the latter must be somewhat darkened. Above all both, eyes are free to aid in copying the real picture, the microscope serving only as a means. For low magnifications a simple kind of vertical device may be used with direct projection without the employment of oculars; for higher magnifications a more complicated apparatus is necessary in order that the compound microscope may be used.

The most usual form of the second type is represented by the Abbé drawing apparatus which is constructed of reflecting prisms and a mirror attached to a long arm.[1] With practice, accurate work may be done with this excellent apparatus but it is done exclusively under monocular vision. In order to make the point of the pencil more easily visible pencils have been constructed which may be illuminated.

IV. The Photography of Microscopical Preparations

Photography, or rather photomicrography may replace the drawing of microscopic preparations. Naturally it has the advantage over a drawing that is afforded by an objective picture. For subjectivity can not be altogether avoided, even in the most careful and accurate drawing. On the other hand photomicrography has the disadvantage of being able to picture only one optical plane. All objects not in this plane appear blurred in the photograph with the result that most photomicrographs, at least those taken under moderately high magnification, do not yield a very clear picture. The thicker the object to be photographed and the higher the magnification, the less favorable are the results of photomicrography. Consequently to make a photomicrograph under high magnification the thinnest possible sections must be selected. From these considerations it is clear that the best photomicrographs will be those which have been taken under the lowest magnification possible, since only by so doing is there any assurance that all parts of a relatively thick section will be sharply pictured. The curvature of the field of most oculars interferes with this result. Consequently in all cases in which photomicrography with an ocular enters into consideration, periplanatic oculars should be employed. But by far the best photomicrographs are obtained of preparations under low magnification and with the aid of the objective alone, only the center of the field of view being utilized. Here also as far as possible objectives should be sought which have a flat field, *e. g.* the so-called microplanar objectives. Increased magnification may be obtained by using a camera with great length of bellows. If large general views are desired, such as could not be brought at one time within the field of the microscope, photomicrography is not merely a substitute for drawing, which would be very time consuming, but even has incalculable advantages over direct microscopic observation.

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[1] For details see catalogues.

The apparatus of photomicrography is extremely simple. Any photographic camera with a bellows may be used if a "light-tight" connection is made between the tube of the microscope and the objective end of the camera. Various designs of photomicrographic apparatus are manufactured, the smaller types which rest on the ocular and have only a short bellows, have, for most histological-embryological studies, scarcely any value beyond that of toys. However there are cases in which success may be attained with such small apparatus which is handy and can be quickly used; *e. g.* in photographing fresh and highly perishable structures. If photomicrography is to be a quick and useful substitute for drawing, only a camera with a long bellows should be used. Because the size of the preparations often is considerable the camera should take a large plate. For further details see special instructions for photomicrography.

Photomicrography can serve a very valuable use if it is made the basis for drawing. This may be done directly or indirectly; for details see publications concerned. Almost all the illustrations of this Atlas have been drawn upon a photomicrographic foundation.

V. The Technique of Microscopical Preparations

Objects from the field of histology or microscopic anatomy are rarely suitable for microscopic examination without previous preparation. Fluids, for example, may be examined microscopically without special treatment, but with the exception of blood and sperm, and as a rule the saliva, their constituents are not subject to morphological determination. In addition the female sex-cells, hairs and some other structures may be examined with the aid of the microscope, either entire or without the necessity of special preparation.

But in the great majority of cases, both human and animal tissues and organs must be prepared by processes of different kinds in order to be rendered suitable for investigation with the microscope. Examination of objects in the "fresh" condition may be distinguished from examination after previous fixation of the tissues. Objects which can rarely be examined in a fresh and living condition may be so dealt with in the "surviving" state; that is tissues etc. may be taken from a freshly killed animal and examined while they yet show all the phenomena of life. For example, ciliated epithelium, ciliary movement etc. may be thus examined. Tissues or portions of organs may be removed post mortem before they have become changed by processes of degeneration and may be examined in indifferent fluids (physiological salt solution, Ringers solution, see p. 3) without the employment of so-called fixing reagents and without staining. For this purpose the tissues must frequently be torn apart; in a few cases they are so thin and transparent that they may be examined under the microscope without being reduced to small pieces (*e. g.* the great omentum and the mesentery, particularly those of the smaller mammals; loose connective tissue, thin-walled organs such as the distended bladder or lung of the frog, etc.). In the great majority of cases the tissues must be reduced to fragments before examination in the fresh condition. This is best accomplished by TEASING; that is by isolating the individual parts of the tissue (muscle fibers, nerve fibers, fat cells etc.) with the aid of fine needles. This method, which is adapted to much wider use than is commonly made of it at the present time, in spite of its primitive character frequently gives far better impressions of the structure of many objects than do the modern fixation methods. The latter methods are usually combined with staining methods, but before employing them an attempt should be made to obtain an idea of the object in its fresh, unfixed condition by means of teasing. Many gland cells, *e. g.* those of the salivary glands, display in the fresh condition structural features, which are decidedly altered in fixed preparations.

In a still more simple manner small pieces of mucous membranes may be cut off and used for the microscopic examination of ciliary movement; adipose tissue and many other varieties of connective tissue, occasionally also cartilage, may be thus prepared for microscopic examination.

If teasing is not sufficient, or if the consistency of the tissue renders impossible this manner of preparation, the fresh tissues or organs must be cut into sufficiently thin slices with the razor, the double razor, or with the aid of the freezing microtome. Fresh, surviving cartilage and many organs which tease badly, may be thus examined and the results obtained by teasing may be compared with the pictures seen in the sections.

Examination in the fresh condition renders possible the employment of different reagents (water, acids, alkalis) on the tissues. Their action on the various constituents of the tissues can only be studied in fresh preparations, which in this regard again take precedence over fixed preparations.

Another mode of investigation of surviving tissue is by the aid of so-called vital dyes, *i. e.* dyes which act on living or surviving tissues. Many of these dyes stain the vital granules, *e. g.* those of histiocytes (p. 55). Others like methylene blue used intravitam, stain nervous tissue. This is a combination of investigation in the fresh condition on the one hand and on the other hand of a staining process such as is usually employed on objects that have been fixed.

Important as is investigation of animal and human tissues in the fresh condition and much as it is to be deplored that this means is so largely neglected, yet it can only give a limited amount of information as to the structure of the organs of the human body. For instance, blood is highly suitable for the most simple form of microscopic examination; however, such investigation will not suffice for the observation of the finer structure of the colorless blood cells. There must be a "FIXATION" of the preparation with subsequent staining in order to obtain the desired information.

By FIXATION of tissues and organs there is understood, in general, the treatment with reagents which precipitate albumins. Among these ethyl alcohol formerly played a large part. The number of methods of fixation, and of chemical substances, and above all of their mixtures in solution, which are employed to-day is exceedingly great. For these, as for all special methods which cannot be discussed here,[1] reference must be made to the handbooks of microscopical technique. As mentioned solutions of different salts (of mercury, chromium, etc.) are usually employed, or alcohol, or formaldehyde in aqueous solution (so-called formol or formalin). In many combinations acetic acid plays an important part. Histological technique does not shrink even from the employment of the noble metals (silver, gold, platinum, osmium) as salts or oxides. The extremely simple method of fixing albumins by heat has been used in methods of staining blood.

Fixation has two purposes in view, first, to preserve the tissues by precipitating their albumins and bringing them to a proper consistency for further treatment; second, to prepare for the use of stains. If the pieces of tissue are sufficiently thin to be observed under the microscope without further subdivision they may be stained after fixation and examined in toto, *i. e.* without being cut into sections. This type of preparation has great advantages over any section for the latter ultimately represents only an expedient. The pictures of mitoses in plate one *(Figs. 3—15)* are not derived from sections but from an epithelial lamella which was brought quite intact under the microscope. In this way the entire mitotic figure is visible, uncut; not just parts of it as would be the case had it been necessary to section the tissue. It is thus by no means an advantage to find that recourse to sections is necessary; it is often a fault to investigate by sections when it is not necessary.

Unfortunately in the majority of cases it is necessary to employ sections. For this purpose a modern sectioning machine or MICROTOME is used. Of these there is an extraordinary variety of construction, of great efficiency. They permit the preparation of uniform sections of any thickness desired down to $1\ \mu$. As a rule the material undergoes a preparation (so-called embedding) before it can be cut into sections by the microtome. Only in the case of the so-called freezing process is treatment such as is demanded by the embedding methods unnecessary. In this process fresh tissues are frozen, usually by liquid carbon dioxide, and in this condition are cut into sections. Although this is a rapid method yet in the technique of normal histology it plays only a subordinate role and is usually preceded by fixation in formalin. In the great majority of cases the METHOD OF EMBEDDING is employed *i. e.* the fixed material, after dehydration in alcohol of increasing strength, is embedded either in paraffin or in celloidin (a solution of nitro-cellulose in alcohol and ether). The material is permeated with the substance which finally is cast in a block surrounding it. In the paraffin embedding process the objects must first pass through a solvent of paraffin (chloroform, xylol, etc.; for details see text books of technique). A combination of the two methods of embedding is possible. Objects embedded in paraffin are cut with a dry knife. (Knives differ greatly in such matters as form, grinding of the edge, etc. according to the type of microtome with which they are used.) Objects embedded in celloidin are cut with a knife kept wet with alcohol. The paraffin sections in further treatment must have the paraffin removed by a paraffin solvent and must then pass through alcohols of diminishing strength before they can be stained in aqueous solutions.

Sections are rarely examined in the unstained condition; usually both celloidin and paraffin sections are stained. Many methods of fixation, such as those with osmic acid (OsO_4) or gold chloride, with subsequent reduction in light, give a certain degree of staining to many tissues; but as a rule special stains are employed. The dyes are obtained in part from the animal kingdom, such as carmine (the staining principle of cochineal);

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[1] See preface.

in part they are vegetable dyes such as haematoxylin, brazilin; but now coal tar dyes (aniline dyes) are usually employed. The number of the dyes, their various solutions, the mixtures of several dyes and the modes of their employment is extremely great. In this Atlas, under the title "Technique" there is given briefly the process employed in the preparations mentioned. This is not the place to undertake the description of the numerous methods of staining; for such matters text books on technique should be consulted.

It must be mentioned however that there are two types of staining; 1. staining "in toto" which is done after fixation but previous to embedding the material, *e. g.* staining in toto with sodium carminate which gives beautiful results, particularly with the central nervous system; 2. staining after sectioning. The stained sections are usually kept as permanent preparations which will remain unchanged for a decade and perhaps much longer. Neutral Canada balsam dissolved in xylol is usually employed for mounting the preparations; the section, or the preparation to be mounted without cutting, must previously be dehydrated in alcohols of increasing strength, after which the alcohol is replaced by xylol.

INDEX.

A.

Accessory band of striated muscle 102
— fiber of motor end plates 177
— lacrimal glands 281
— nasal cavities 222
— thyroid glands 229
Acervulus cerebri 172
Achromatic elements, of nucleus 10
— of mitotic spindle 24
— — origin of 25
Acinus = alveolus 48
Acrosome = perforatorium 242
Adamantoblasts 188
Adenoid tissue 72
Adipose tissue 68
— serous variety of 71
Adrenal gland 177, 258
— vessels and nerves of 260
— chromaffine (phaeochrome) granules of 260
— lipoid granules of 259
Adrenalin 260
Adventitia = tunica adventitia (q. v.)
Agglutination, of blood corpuscles 83
— of sperms 245
Agminated follicles Peyer's patches 211
Air cells = alveoli (of lungs) 226
Albuginea = tunica albuginea (q. v.)
Alimentary canal, wall of 182
Allophores 17
Altmann's theory of protoplasmic structure 4
Alveolar, duct 225
— glands 48
— theory of protoplasmic structure 4
Alveoli 48
— of lungs 226
Amacrine cells 271
Ameloblasts 188
Amitosis 19
Amoeboid movement 18
Amphiaster = diaster 26
Amphicytes 119, 176
Amphipyrenin 10
Ampullae, of semicircular canals 284
— of ductus deferens 246
— of oviduct 254
Anaphase 26
Anisotropic structures 59, 76, 102, 278
Annuli fibrosi 78, 142
Annulus fibrocartilagineus 290
Aorta 144
Apocrine secretion 43
Aponeurosis 67, 160
— pharyngis 205
Appendices epiploicae 69
Appendix epididymidis 247
— testis 247
— vermiformis 211
Aqueous humor 267
Arachnoid membrane 173
— trabeculae 65
Archiplasm (archoplasm) 7
Arciform fibers 262
Areola 310
Areolar connective tissue 64
Argyrophile fibers 60
Arnold's granules 8
Arrector pili muscle 303
Arteria centralis retinae 277
— pulmonalis 144
Arteriae afferentes 234
  arciformes 234
  bronchiales 227
  interlobulares 234
  nutriceae 133
Arteries 143
— arcuate 234
— bronchial 227
— central, of splenic corpuscles 153
Arteries classification of 143
  coats of 143
  of cranial cavity 145
  of large size 144
  — of medium size 144
  nerves of 145
  precapillary arterioles 143
  sheathed 154
  — of small size 144
  special features of 144, 145
  umbilical 145
  — vasa vasorum 145
Arteriolae rectae 234
Arteriole 143
Articular cartilages 78, 133
Articulations 140
Arytenoid cartilages 223
Asbestiform (amiantine) degeneration (structure) 74, 75, 134
Astral rays 24
Astrocytes 128, 129
— foot plates of 129
Astrosphere 24
Atresia, follicular 253
Atrium, wall of 110
Atrio-ventricular bundle, fibers of 110
Auditory meatus (passage), external 293
  ossicles 291
  strings (cords, fibers) of Corti 287
— teeth of Huschke 286
Auerbach, plexus of 212
Auricle 293
Axial thread of sperm 243
Axillary artery 144
Axis cylinder 124
Axones 112
  collaterals of 112, 113
  cone of origin of 112
  medullated (myelinated) 123
  naked 123
— non-medullated 127
Axoplasma = neuroplasma 115

B.

Baillarger, line of 168
Bartholin, glands of 258
Basal corpuscles 13, 40
— membrane 60, 61
— filaments 5, 42, 196, 218, 231
Basichromatin 11
Basket cells, of glands 51, 195
— of cerebellum 169
Basilar membrane 287
Basophilic leucocytes 89
Basophily of hyaline cartilage 75
Bergmann, cells (fibers) of 171
Bichat, fat pods of 69
Bile capillaries 216
— ducts 217
— pigment 213
Bioblasts 4
Bipolar nerve cells 119, 271
Bizzozero, platelets of 90
Bladder, gall 217
— urinary 236
Blepharosomes 40
Blood 82
— clotting of 91
— corpuscles 82
— — colorless (white) 86
— — red (erythrocytes) 82
— dust 91
— plasma 82
— platelets (thrombocytes) 90
— vessels 141
— — arteries 143
— — capillaries 147
— — development of 148
— — veins 145
Bone (as organ) 131
— canals, Haversian 131
— — of Volkmann 132
— cancellous (spongy) 131
compact 131
— development of, endochondral 136
— — intramembranous 138
— — perichondral 137
— growth of 138, 139
— lamellae, circumferential (ground) 132
— — Haversian 80, 132
— — interstitial 132
— marrow 134
— Sharpey's fibers 133, 140
Bone vessels and nerves of 134
— tissue 78
— canaliculi 79
— capsules 80
— chemical constitution of 78
— fibers 79, 80
— lacunae 79
— matrix 80
— osteoblasts 81
— osteoclasts 81
— osteocytes 79
— resorption of 81
Bowman, capsule of 230
— discs and sarcous elements of 102
— glands of 222
— membrane of 261
Brain sand 172
Bridges, intercellular 31
Broad ligament, vestigial remains in 254
— relation to muscle of oviduct and uterus 255, 257
Bronchi 223, 224
Bronchioles 225
— respiratory 225
Brownian movement 87, 200
Bruch, membrane of 265
Brunner, glands of 210
Brush border 39, 231
Buds of Schmidt 229
Bulb of hair 302
Bulbo-urethral glands 238
Bundle, atrio-ventricular 110
Burdach, funiculus of 163
Bursae 160

C.

Call-Exner bodies 251
Canal(s), central of spinal cord 162
corneal 262
dentinal 185
Haversian 131, 139
— nutrient 133
of Petit 280
of Schlemm 263
taste 294
of Volkmann 132
Cajal, cells of 164
Calcification of cartilage 76
— of tooth 180, 191
Calyces of renal pelvis 235
Cambium layer of periosteum 137
Canaliculi, of bone 79
— of Golgi 6
— — secretion 45
Capillaries, bile 216
— blood 141, 147
— lymphatic 149
— nerves of 148
Capsule(s) of Bowman 230
— connective-tissue 67
— hepatic, of Glisson 213
— of joints 140
— of lens 278
— of lymph glands 149
— of nerve cells 176
renal 233
— splenic 152
Cardiac glands 206, 208
— muscle 107
— — nerve terminations in 178
Carotid, artery 144
— gland 177, 260
Cartilage 72
— asbestiform (amiantine) degeneration (structure) of 74, 75, 134
— calcification of 76
— capsules 75
— cells 74
— cellular 78
— chondrin 73
— chondroitin-sulphuric acid 73
— chondrones 75
— development of 76
— elastic 77
— fibro-cartilage 77
— growth of 76
— hyaline 73
— lacunae 74
— matrix 73, 74
— perichondrium 75
Cartilages, articular 133
— bronchial and tracheal 224
— epiphyseal 139
— of larynx 223
— of ribs 134
Cavernous tissue of penis 247
Cell, the 1—32
— amitosis 19
— centrosome 2, 12
— chromidia 5

Cell chromosomes 21
— cilia 39
constituents of 2
cuticula 14
cytoplasm 2, 3
cytosome 2
division, direct 19
— indirect (karyokinetic) 20
— in maturation of germ cells 28, 241
granules of 7
inclusions 3
karyokinesis (mitosis) 20
kinetic organ of 12, 40
life and death of 29
membrane 3, 14
microsomes 4
mitochondria 4
movement, amoeboid 18
— ciliary 41
non-nucleated 2
nucleolus 11
nucleo-plasmatic relation 2, 9
occasional constituents of 14
organs of 2
paraplasm 5
pellicula 14
phenomena of life of 18—29
pigment in 8
plastosomes 4
protoplasm 2
reproduction of 19
resting phase 3
reticular apparatus 2, 5
shape of 1, 2
size of 2
trophospongium 6
Cell nests, of cartilage 75
nets 31
Cells, of adipose tissue (fat) 68
air 226
amacrine 271
amphicytes 119, 176
astrocytes 128
basket, of glands 51, 195, 197
— of cerebellum 169
of Bergmann 171
bipolar 119, 271
blood, red 82
— colorless (white) 86
bone 79
of Cajal 164
Cells, cartilage 74
centro-acinar 219
chief, of gastric glands 207
— of thyroid gland 228
chromaffine 121, 177, 260
chromophile and chromophobe 172
ciliated 39
clasmatocytes 55
of Claudius 289
colloid 228
columnar 1
commissural 163
cone 273
connections between 30
connective-tissue, fixed 53
— wandering 45
cortical, large and small 169
daughter 27, 28
Deiters', astrocytes 128
— nerve 113, 116
— of organ of Corti 228
— phalangeal 288
enamel 188
endothelial 94, 95
ependymal 128, 162
epithelial 32
erythroblasts 91
erythrocytes 82
fibroblasts 54
fibrocytes 53
free 2
giant 20, 93, 257
glandular 42—51
goblet 43
of Golgi, types I and II 113
granular, large 171
— small 115, 118, 171
granulocytes 89, 90
hair 285, 288
Hensen's 289
of Hortega 129
horizontal 271
interstitial, of gonads 47
— of ovary 252
— of testis 238
intrinsic, of spinal cord 163
of Kupffer (stellate) 216
of Langerhans, epidermal 297
— pancreatic 218
lemmocytes 176
leucocytes 86—90
Cells, lutein 252
lymphoblasts 149
lymphocytes 88
macrophages 90
mantle 119
marrow 91
mast 56, 89
megakaryocytes 13, 15, 20, 93
megaloblasts 91
megalocytes 93
microcytes 83, 129, 130
microphages 90
mitral 117
monocytes 89
motor nerve cells 161
mucous 194
of Müller (fibers) 269
multinucleate, formation of 20
muscle 96
myelocytes 92, 115
nerve 111
— classification of 112
neuroblasts 110
neuro-epithelial 119
neuroglia 128
normoblasts 91
normocytes 83
olfactory 295
osteoblasts 81, 136, 138
osteoclasts 81, 136
osteocytes 79
ovum 250, 251, 253
oxyntic (parietal) 207
of Paneth 209
phaeochrome 121, 177, 260
phagocytes 19, 55, 89
phalangeal (of Deiters) 288
pigment 57
plasma 56
polymorphous 118, 164
prickle 296
of Purkinje 117, 169
pyramidal 117, 163
reticulo-endothelial 95
rod, of retina 272
— of Corti 287
of Rouget 147
satellite 129
of Schwann 127, 176
secretion in 42—46
serous 194
of Sertoli 239

Cells, spermatogenic 240
— spongioblasts 110
— squamous 33
— stellate, of Kupffer 216
— tactile, of Merkel 179, 180
— tendon wing-cells 67
— thread 284
— thrombocytes 91
— tract 161
— visual 271
— wandering 54
Cellulae radiculares 161
— funiculares 161
Cement, of lamellar bone 132
— intercellular 30
— of tooth 184, 186
Central, artery of splenic corpuscles 153
— canal of spinal cord 162
— gray matter of brain 163
— nervous system 160
— — cerebellum 168
— — cerebral cortex 163
— — membranes of 172
— — spinal cord 160
— — vessels of 172
— spindle of mitosis 24
— vein of hepatic lobule 214
Centro-acinar cells 218
Centrosome 12
— radiation from 24
Centrosphere 13
Cerebellum, cortex of 168
— granular layer 170
— molecular layer 169
— fibers 171
— granular cells 115, 118, 171
— Purkinje cells 117, 169
Cerebral cortex 163
— cells of 163
— cyto-architecture 167
— layers of 164
— — medullated fibers of 167
— myelo-architecture 168
— types of 167
Cerebrospinal ganglia 176
Ceruminous glands 293
Cervix uteri 255, 256
Cheeks 184
Chief cells, of gastric glands 207
— of thyroid gland 228
Chondroitin-sulphuric acid 73
Chondrin 73
Chondriocontes 4
Chondriome 4
Chondriomitomes 4
Chondriosomes 4
Chondrone 75
Chordae tendineae 142
Chorioid coat of eyeball 264
— ciliary body and processes 265
— iris 265
— laminae 264
— membrane, of Bruch 265
— — hyaline (vitreous) 264
— tapetum 264
— vessels and nerves of 267
Chromaffine cells 121, 177, 260
Chromatin 9, 11
— in resting nucleus 10
Chromatolysis 29
Chromic acid and chromates, effect on chromaffine cells 177
Chromidia 5
Chromioles 11, 22
Chromomeres 22
Chromosomes 21
— individuality of 27
— numerical relations 22, 28, 241
— polar arrangement 21
— significance 27
Cilia 39
— of eyelid 280
Ciliary arteries 267
— body 265
— movement 41
— muscle 265
— nerves 264
— processes 265
Ciliated epithelium, stratified 37
Circumferential (ground) lamellae 132
Circumvallate (vallate) papillae 201
Clark, column of 161, 163
Clasmatocytes 55
Claudius, cells of 289
Climbing fibers of cerebellum 171
Clitoris 258
Coal dust in lung 226
Cochlear duct, general 285—286
— organ of Corti 287—289
— vessels of 290
Coeliac artery 144
Cohnheim's areas 103
Collagenous fibers 58
Collaterals of axones 112
Collecting tubules of kidney 233
Colloid 47
— in hypophysis 172
— in thyroid gland 228
Colon 210
Colostrum corpuscles 209
Column of Clark 161, 163
Commissural cells 161, 163
Compact bone 131
Cone fibers and granules 273
— of origin of axone 112
Cones of retina 274
Conjunctiva 221
Connections between cells 30
Connecting-piece of sperm 242
Connective tissue 52
— adipose (fat) 68
— areolar 64
— bone 78
— bundles of 58
— cartilage 72
— cells of 53—58
— classification of 53, 62
— development of 52
— elastic 68
— embryonic (mesenchyme) 52
— fibers of 58—62
— gelatinous 62
— ground substance 62
— of inner meninges 65
— loose (unformed) 63
— proper 53
— pigmented 62
— of serous membranes 64
— tendinous 66
Convoluted tubules of kidney 231, 233
Cords, of Corti (strings) 287
— vocal 223
Corium 296, 298
Cornea 261
Corneal corpuscles 262
— endothelium 262
Cornification 30, 42
Corona radiata 250
— ciliaris 265
Corpora amylacea 237
— cavernosa 247
Corpus albicans 253

Corpus cavernosum urethrae 247
— Highmori 238
— luteum 252
— — degeneration of 253
— — spurium (menstruationis) 253
— spongiosum of female urethra 236
Corpuscles, basal 13
— blood 82, 86
— corneal 262
— genital 182
— Golgi-Mazzoni 182
— of Grandry 180
— of Hassall (thymic) 157
— of Herbst 181
— lamellar 181
— of Meissner 180
— renal, of Malpighi 230
— of Ruffini 179
— salivary 200
— splenic, of Malpighi 152
— tactile 180
— Vater-Pacinian 181
— of Wagner 180
Corpuscula arenacea 172
Corti, organ of 287
Cowper, glands of 238
Crenation of erythrocytes 84
Crescents of Ebner (or of Gianuzzi) 194, 197
— of exhaustion 195
Crista basilaris 286
— spiralis 286
Cristae acusticae (ampullares) 284
Crosses of Ranvier 126
Crusta 7
Crypts of Lieberkuhn 209
— tonsillar 204
Crystalloids of interstitial cells 238
Crystals, haematoidin in ovary 253
— of Lubarsch and of Spangaro 238
— of oleo-margarin 70
Cumulus ovigerus 250
Cupula of cochlear duct 285
Cupula of crista acustica 285
Cutaneous glands 306
Cuticula 14
— dentis 186
— of hair 301
Cuticular border 39
Cutis 296
Cylindro-conic segments of nerve fibers 126
Cytochromatin 115
Cytoplasm 3
— theories of structure of 3, 4

D.

Daughter asters 26
— cells 27
— nuclei, formation of 27
Decalcification of bone 78
Deiters, astrocytes of 128
— nerve cells of 113, 116
— phalangeal cells of 288
Demilunes = crescents 194, 197
Dendrites 112, 117, 122
Dental ledge 187
— papilla 187
— pulp 184, 193
— sac 193
— vessels and nerves 187
Dentinal canals 185
— fibers 184, 185
— sheath, of Neumann 185
Dentine 184, 185
— development of 189
— secondary 193
Derma 296
Descemet, endothelium of 262
— membrane of 262
Deutoplasm 251
Development of bone 135
— endochondral 136
— intramembranous 138
— perichondral 137
Diaster 26
Digestive tract, general 182
Dilator muscle of pupil 266
Diplosome 13
Discus proligerus (oöphorus) 250
Disc of Bowman 102
— tactile 180
Dispireme 26
Dopa reaction 17, 299
Dorsal nucleus of spinal cord 161
Double refraction in bone 80
— in collagenous fibers 59
— in hyaline cartilage 76
— in muscle 97, 101
— of myelin 124
Duct(s), alveolar 225
— bile 214, 217
— cochlear 285
— ejaculatory 246
— excretory 195
— of Gärtner 258
— intercalated (intermediate) 49, 195
— lacrimal 282
— Müllerian 255
— naso-lacrimal 283
— of ovary 254
— of pancreas 218
— papillary 236
— of parotid gland 197
— salivary (secretory) 196
— seminal 244
— sublingual 198
— submaxillary 198
— thyreo-glossal 228
— Wolffian 258
Ductless glands 47
Ductuli aberrantes testis 247
— efferentes testis 244
Ductus cochlearis 285
— deferens 245
— — ampulla of 246
— ejaculatorius 246
— epididymidis 245
Duodenum 210
Dura mater 67, 172

E.

Ear, external 293
— internal 283
— — cochlea 285
— — cristae and maculae 284
— — organ of Corti 287
— middle (tympanum) 291
— — tympanic membrane 290
— wax (cerumen) 293
Ebner, crescents of 194
— glands of 195, 197
Eccrine secretion 43
Ectoplasm 7
Egg-tubes of Pflüger 250
Elastic cartilage 77
— fibers 59
— membranes (fenestrated) 60, 68
— tissue 68
Elastin 60

Eleidin 42, 297
Ellipsoids 274
Enamel 32, 184
— cells, inner (adamantoblasts) 188
— chemical composition of 186
— cord 188
— development of 188
— fibers or prisms 185
— furrows 188
— knot 188
— ledge 187
— lines of Retzius 186
— — of Schreger 186
— organ 187
— pulp 188
— theories of formation 191
— Tomes' processes 189
— umbilicus 188
End bulbs 181
End plate 120
Endocardium 142
Endocrine glands 46, 47
Endolymph 283
Endoneurium 175
Endoplasm 7
Endothelium 93, 141
— Descemet's, of cornea 262
— of iris 266
— meaning of the term 94
— syncytial 95
— of vascular system 95
Eosin bodies 171
Eosinophile leucocytes 54
Ependymal glia 111, 128
Epicardium 142
Epidermis 296
— mitosis in cells of 297
— pigment in 298
Epididymis 244
Epiglottis 223
Epimysium 158
Epineurium 175
Epiphyseal line 137, 139
Epiphyses of bones 139
— ossification of 137, 139
— vessels of 134
Epiphysis cerebri 172
Epithelial corpuscle type of glands 61
Epithelium 32
— ciliated 34, 37
Epithelium cuticular border 39
— ependymal 111, 173
— follicular, of ovary 249
— germinal 249
— glandular 42
— intercellular bridges 31, 296
— mesothelium 94
— pavement 34
— pigmented, of retina 267
— respiratory 225
— secretion by cells of 42
— simple 33
— special differentiations of cells of 39
— stratified 34
— superficial 33—42
— transitional 36, 235
Eponychium 305
Epoöphoron 254
Equation division 28
Equatorial plate 24, 27
Erectile (cavernous) tissue 247
Erythroblasts 91
Erythrocytes 82
— crenation of 84
— haemolysis 85
— megalocytes 83
— microcytes 83
— shape of 83, 86
— size of 83, 85, 86
Eustachian tube 292
Excretion, definition of 43
Excretory ducts 195
Exocrine glands 46, 47, 48
External, ear 293
— acoustic meatus 293
Eye 261
— lid 280
— lacrimal apparatus 282
— optic nerve and papilla 277
Eyeball 261
— aqueous humor 267
— chorioid coat 264
— ciliary body 265
— coats of 261
— cornea 261
— iris 265
— lens 278
— pigmentary epithelium 268
— retina 269
— — pars optica 269
— — pars caeca 276
Eyeball sclera 262
— uvea 264
— vitreous humor 279
Eyelashes 280
Eyelids 280
— conjunctiva 281
— vessels and nerves of 282

F.

Fallopian tube (oviduct) 254
Fascia 67, 160
— linguae 200
Fat 71
— atrophy of 69
— cells 70
— — origin of 70
— — serous 71
— droplets as cell inclusions 42, 70
— lobule of 70
— pads of Bichat 69
— tissue 67
Fatty acids, crystals of 69
Femoral artery 144
Fenestrated (elastic) membrane 60, 68
Fenestration of nerve cells 118, 120
Fiber baskets of retina 270, 273
Fiber layer of Henle 271
Fibers, arciform 262
— (cells) of Bergmann 171
— in bone 79
— in cartilage 73, 74
— central spindle 24
— climbing 171
— collagenous 58
— of connective tissue 58
— dentinal 185
— elastic 59
— elementary 31
— enamel 185
— inter- and intra-geminal 294
— of Korff 189
— of lens 279
— mantle (traction) 24
— mossy 171
— of Müller 269
— muscle, cardiac 107
— — smooth 96
— — striated 99

Fibers, nerve 111, 122
— of neuroglia 129
— pre-collagenous 60
— pre-elastic 62
— of Remak 127
— of reticulum 60
— of Sharpey 133, 140
— tangential 164, 168
— ultraterminal 178
Fibroblasts 54
Fibrocytes 53
Fibro-cartilage 77
Fibro-elastica of periosteum 133
Filar theory of protoplasmic structure 3
Filaments, basal 5, 42, 196, 218, 231
Fissure, anterior median 163
Flagellum 41
Flemming, theory of protoplasmic structure 3
Foam theory of protoplasmic structure 4
Folds of Kerkring 210
Foliate papilla 202
Follicle of hair 302
Follicles, agminated 151
— Graafian 249
— — number of 253
— — primordial (primitive) 250
— — rupture of 252
— lingual 202
— solitary 211
— of thyroid gland 228
Follicular atresia 253
Folliculi vesiculosi 249, 250
Fontana, spaces of 267
Foot plates of astrocytes 129
Foramen caecum linguae 203
Formed connective tissue 65
Fornix conjunctiva 281
Fossa navicularis 248
Fovea centralis 275
— externa 275
Foveolae gastricae 206
Free nerve-endings 178
Fromann's lines 126
Fundus (gastric), glands of 207
Fungiform papillae 201
Funiculus, of nerves 175
Funiculi of spinal cord 163
Fuscin 15, 16

G.

Gall bladder 217
Ganglia, of brain 163
— connective tissue in 176
— structure of peripheral, cerebrospinal 176
— — sympathetic 176
Ganglion cells 112
— nervi optici 270
— retinae 271
— spiral 289, 290
Gärtner, duct of 258
Gastric crypts 206
— glands 207
— vessels and nerves 212
Genital, corpuscles 182
— organs, female 249
— — male 237
— — vestigial structures in 247, 254, 258
Gennari line of 168
Germ layers 1, 32, 52, 99, 110
Germinal epithelium 249
— spot and vesicle 11, 251
Giant cells of bone marrow 93
— of vagina 257
— pyramidal cells 164, 165, 167
Gianuzzi, crescents of 194, 197
Giraldés, organ of 247
Glands 46
— accessory thyroid 229
— adrenal (suprarenal) 258
— alveolar 48
— basket-cells of 51, 195
— of Bowman 222
— of Brunner 210
— buccal 198
— bulbo-urethral of Bartholin 258
— caecal 210
— cardiac 206, 208
— carotid 260
— ceruminous 293
— of cheeks 184
— classification of 49
— corpus luteum 252
— Cowper's 238
— duct system of 48
— ductless 47
— duodenal 210
— of Ebner 197
— endocrine 46, 47
Glands endo-epithelial 48
— exocrine 46, 47, 48
— exo-epithelial 48
— of external secretion (exocrine) 46, 47, 48
— of fundus (gastric) 207
— of gall bladder 218
— gastric 207
— general structure of 49
— haemolymph 156
— of internal secretion 47
— intestinal 209
— kidney 229
— of Krause 281
— labial 184
— lacrimal 282
— of Lieberkühn 209
— lingual 202
— of Littré 248
— liver 212
— lymph 149
— mammary 309
— Meibomian 281
— mixed 197
— of Moll 280
— Montgomery's 310
— mucous 197
— nasal 221
— of Nuhn 203
— of oesophagus 205, 206
— olfactory, of Bowman 222
— of oral cavity 193, 198
— ovary 249
— pancreas 218
— paraganglia 177
— parathyreoid 229
— parotid 196
— parenchyma of 46
— pineal 172
— praeputial (of Tyson) 247
— prostate 237
— pyloric 208
— reproductive 50
— — female 249
— — male 237
— reticular 50
— salivary 193, 196
— sebaceous 306
— secreting parts of 51
— serous 196
— stroma of 46
— sublingual 198

Glands submaxillary 197
— sudoriparous or sweat 307
— suprarenal (adrenal) 258
— tarsal 281
thymus 156
— thyroid 228
— — accessory 229
tubular 48
— tubulo-alveolar 48
— Tyson's 247
— uterine 255, 256
of urinary bladder 236
— vestibular 258
— of Zeiss 280
Glandulae ciliares 280
— clausae 46
— dehiscens 51
— evihentes 46
— tartaricae 191
Glans penis 249
Glia cells 128
— ependymal 128
— fibers 129
— of retina 270
Gliopil 129
Glisson, capsule of 213
Glomerulus, renal 230
Glomus caroticum 260
Glycogen in liver 213
Goblet cells, function of 43
— of large intestine 210
— of small intestine 209
Golgi, apparatus of 5
— nerve cells, types I and II 113
Golgi-Mazzoni corpuscles 182
Goll, funiculus of 163
Graafian follicles 249, 250
— atresia of 253
— number of 253
— primordial (primitive) 250
— rupture of 252
— theca folliculi 250
Grandry, corpuscles of 180
Granular cells of cerebellum 115, 118, 171
— layer of Tomes 185
— theory of protoplasmic structure (Altmann) 4
Granules of Arnold 8
— of cells 5, 7
— chromaffine or phaeochrome 260
Granules lipoid 8
— pigment 8
— secretion 8, 43
— zymogen 8
Granulocytes 89
Gray matter of spinal cord 111, 161
Great omentum 220
Ground, bundles of spinal cord 163
— lamellae of bone 132
— substance of connective tissue 62
Guanine pigment 17
Guanophores 17
Gums 183
Gyri structure of certain 167

H.

Haematoidin 17, 253
Haematoconia 91
Haemocytoblasts 92
Haemoglobin 84
Haemolymph glands 156
Haemolysis 85
Hair 300
— arrector pili muscle 303
— body hairs 303
— bulb 302
canal 303
cells of internal ear 285, 288
club 304
cone 303
cortex 300
cuticle 301
development of 303
duration of life of 304
eyelashes 304
follicle 302
glands of 306
growth of 303
Henle's layer 301
Huxley's layer 301
hyaline membrane 302
lanugo 303
medulla 301
papilla 300, 303
pigment 300
replacement 304
rings 300
root 301
Hair root sheath, inner 301
— — — outer 302
— sebaceous glands of 306
— shaft of 300
— shedding of 304
— vessels and nerves of 302
Hassall's corpuscles 157
Haversian canals 131
— development of 138
— lamellae and systems 132
Heart 142
— annuli fibrosi 142
— muscle 107
— — of atrium 110
— valves of 142
— vessels and nerves of 142, 178
Heidenhain, theory of structure of striated muscle 106
Hemiganglia 177
Henle, fiber layer of 271, 273
— layer of 301
— loop of 230, 231
— sheath of 175
Hensen, cells of 289
— line of 101
Hepatic lobule 213
— bile capillaries of 216
— central vein of 214
— circulation of blood in 214
Herbst, corpuscles of 181
Highmore's body 238
Histioblasts 96
Histiocytes 55, 96
Holmgren's trophospongium 6
Holocrine secretion 43
Horizontal cells of retina 271
Hormones 47
Hortega cells 129, 130
Howship's lacunae 81
Huschke, auditory teeth of 286
Hyaline cartilage 73
— membrane, of hair follicle 302
— of ovarian follicle 251
Hyaloid canal 280
— membrane 279
Hydatid, of Morgagni 247
— stalked 247
Hymen 258
Hypophysis cerebri (pituitary body) 171

I.

Immigration theory of thymus 156
Incisures of Schmidt-Lanterman 125
Inferior paracentral lobule 167
Insula 167
Intercalated, ducts 49, 195
— discs 109
Intercellular bridges 31
— cement 30
Interfilar substance of cells 3
Intergeminal fibers 294
Interglobular spaces 185
Internal ear 283
— vessels of 290
Interradiary plexus 168
Interrenal organs 259
Interstitial cells of ovary 252
— of reproductive glands 58
— of testis 238
lamellae of bone 132
— tissue of kidney 233
Intervertebral disc 78, 140
Intestine, large 210
— lymphatic structures of 211
— small 209
— vessels and nerves 212
Intima, of arteries 143, 144
— of veins 146
Intrageminal fibers 294
Intramembranous ossification 138
Intrinsic cells of spinal cord 162
Iris 265
angle of 266
dilator membrane of 269
endothelium of 266
muscles of 266
pectinate ligament of 267
vessels and nerves of 266, 267
Islands of Langerhans 219
Isotropic substance 102

J.

Joints 140

K.

Karyokinesis 20
Karyolysis 29, 253
Keratohyalin 42, 296, 297
Keratin 297
— formation of 42
Kerkring's folds 210
Kidney 229
calyces 235
capsule of 229
— corpuscles of Malpighi 230
— ducts of 235
interstitial connective tissue of 233
lobules 234
papilla 236
pelvis 235
tubules of 229
vessels and nerves 234, 235
Kinetic organ of cell 12, 40
Kinocilia 39
Kinoplasm 7
„Klumpenzellen“ 269
Kölliker, muscle columns of 103
Korff, fibers of 189
Krause, glands of 281
— intermediate line of 101
— theory of structure of striated muscle 106
Kupffer, cells of 216

L.

Labia majora and minora 258
Labial glands 184
Labium tympanicum 286
— vestibulare 286
Labra glenoidalia 78
Labyrinths, membraneous and osseus, vessels of 290
Lacrimal apparatus 282
Lacteal of intestinal villus 209
Lacunae, of bone 79
— of cartilage 74
— Howship's 81
— urethral of Morgagni 248
Lamellae, of bone 80, 132
— of cornea 262
Lamina basilaris 285
— basalis choroideae 264
bony spiral 285
— choriocapillaris 264
cribrosa sclerae 263, 278
elastica posterior, of Descemet 262
fusca sclerae (suprachorioidea) 263, 264
membranous spiral 285
reticularis 289
Lamina vasculosa 264
Laminae chorioideae epitheliales 111
Langerhans, centro-acinar cells of 218
— epidermal cells of 297
— islands of 219
Lanugo hairs 303
Large intestine 210
Larynx 222
— cartilages of 223
— vessels and nerves of 223
Layers of cerebral cortex 164
— of cerebellar cortex 169
Lemmocytes 176
Lens 278
Leptothrix buccalis 200
Leucocytes 89
— basophilic 89
— eosinophilic (oxyphilic) 89
— granulocytes 88
large mononuclear 89
— lymphocytes 88
neutrophilic, polymorphonuclear 89
origin of 90
size of 87
Lieberkühn, crypts (glands) of 209
Ligament, broad 254, 255, 257
— capsular 140
Ligamenta ductum et sacculorum 283
— subflava 68
Ligamentum nuchae 68
— pectinatum iridis 262, 267
— spirale 286
— vocale 68
Limbus spiralis 286
Line(s) of Baillarger 168
of Fromann 126
of Gennari 168
of Hensen 111
of Krause 101
of Retzius 186
— of Schreger 186
— of Vicq d'Azyr 168
Lingual follicles 202
— glands 202
Linin 10
Lips 183
Lipochrome pigment 17

Lipofuscin 16, 119
Lipoid granules (droplets) 213, 252, 259
Lipophores 17
Liquor, cerebrospinalis internis 173
— externis 174
— folliculi 250
Littré, glands of 248
Liver 212
capsule of Glisson 213
— cells and cords of 213
— central veins 214
— duct system 217
— hepatic artery, branches of 214, 416
— lobule 213
— lymphatics and nerves of 217
— portal vein, branches of 214, 215
— reticulum 216
— sublobular vein 215
Lobule, paracentral 164
Locus caeruleus 116
Long-rayed neuroglia 129
Loop of Henle 230, 231
Loose connective tissue 63
Lubarsch, crystals of 238
Lung 224
— air cells (alveoli) 225
— alveolar ducts 225, 226
— bronchi 223, 224
— bronchioles 225
— respiratory 225
elastic tissue of 226
— lobule of 226
— pigment in 226
— pleura 228
— vessels and nerves of 227
Lunula 305
Lutein 252
— cells 252
Lymph, follicles (nodules) 149, 151, 152, 204, 211
— — germinal centers of 149
— gland (node) 149
— sinus 150
— vessel of 151
Lymphatic system 148
Lymphoblasts 149
— lymphocytes 88
— lymphoid tissue 72

M.

Macrophages 90
Macula acustica 283
— germinativa 251
— flava of vocal cords 223
— fovea centralis 275
— lutea 275
Maculo-papillary bundle of retina 270, 278
Malpighi, corpuscles of, renal 230
— — — splenic 152
— stratum muscosum of 296
Mammary gland 309
— areola of 310
— vessels and nerves of 310
Mantle fibers 24
Marrow 134
— gelatinous 134
— primary 136
red cells of 91
— yellow cells of 134
Mast cells of connective tissue 56
— — of blood 89
Matrix of bone 79
— of cartilage 74
— of nail 305
Maturation of ova 251
— of sperms 241
Meatus, external auditory 293
Media of arteries 143, 144, 145
— of lymphatic vessels 148
— of veins 146
Mediastinum testis 238
Medulla of hair 301
— oblongata 163
Medullary cords, of broad ligament 254
— — of lymph gland 149
— rays 230
— sheath 124
Medullated nerve fibers, of cerebral cortex 167
— — — of cerebellum 171
Megakaryocytes 13, 15, 20, 93
Megaloblasts 91
Megalocytes 83
Meibomian glands 281
Meissner, corpuscles of 180
— plexus of 212
Melanin 15
Melanophores 17
Membrana basilaris 287
Membrana elastica externa 144
— — interna 143
— laryngis 223
— pellucida 250
— praeformativa 189
— propria 61
— reticularis 289
— tectoria 286
— vestibularis 285
Membrane, anterior elastic (Bowman's) 261
— basal 60, 61
of Bruch 265
— cell 3, 14
— dilator, of iris 269
— elastic (fenestrated) 60
— elementary 32
enamel 186
— of fat cells 70
— hyaline (vitreous) 61, 264, 302
otolithic 284
of Reissner 285
serous 220
— Shrapnel's 291
synovial 140
— tympanic 290
Membranellae 38, 61, 98
Membranes, of central nervous system 172
— fenestrated 60, 68
Membraneous cochlea 285
— labyrinth 283
— spiral lamina 285
Meninges 172
— vessels and nerves of 174
Meniscus, tactile 180
Merkel, tactile cells of 179
Merocrine secretion 43
Mesenchyme 52
Mesophragma 101
Mesothelium 94
Metakinesis 25
Metaphase 25
Microcytes 83, 129, 130
Microglia 129
Microphages 90
Microsomes 4
Middle ear 291
Milk 310
— secretion of 309
— spots 220
Mitochondria 4

Mitome 3
Mitosis 20
— — anaphase 26
— — diaster 26
dispireme 26
duration of 29
metakinesis 25
metaphase 25
— — monaster 24
prophase 21
spireme 21
telophase 28
Mixed glands 193, 197
Moll, glands of 280
Monaster 24
Mongolian spot 299
Monocytes 89
Mononuclear leucocytes 89
Monospireme 21
Montgomery, glands of 310
Morgagni, hydatid of 247
Mossy fibers of cerebellum 171
Motor, cells of anterior horn 161
— end plates 177
Mouth 183
Movement, amoeboid 18
— Brownian 87, 200
— ciliary 41
Mucinogen (premucin), granules of 44
Mucous, coat of digestive tract 182
— glands 197
Mucus, secretion of 44
Müller, fibers of 269
— reticulum of 268
Multipolar nerve cells 116
Muscle(s) 158
arrectori pili 303
ciliary (of accommodation) 265
columns of Kölliker 103
discs 102
nerve terminations in 177, 178
as organ 158
red and white 104
spindles 159, 179
vessels and nerves of 159
Muscular tissue 96
— cardiac 107
— — bright lines (intercalated discs) 109, 110
— — fibers of Purkinje 110
— — as syncytium 109
Muscular cardiae fibrils of 97, 102, 108
— — smooth 96
— — — distribution of 97
fibers 97, 98
— histogenesis 99
— — membranellae 98
striated 99
— contraction of 107
dark and light fibers 104
— fibers 99
— Cohnheim's areas 103
columns of Kölliker 103
ends of 100, 106
— nuclei 104
— sarcolemma 101, 105
sarcoplasm 103
striation 101
— histogenesis 107
Muscular system 158
Muscularis mucosae of digestive tract 182
Mycelia 200
Myelin 124
Myelo-architecture of cerebral cortex 168
Myelocytes 92, 155
Myoblasts 107
Myocardium 142
Myo-epithelium 38
Myofibrils 5, 81
Myosepta 107

N.

Nabothi, ovula 256
Nail bed 305
Nails 305
Nasal cavities 221
— — accessory 222
— glands of Bowman 222
— mucous membrane 221
Naso-lacrimal duct 283
Nerve cell, see Neurone 111
Nerve cells 111
— amacrine 271
— amphicytes 119, 176
— basket 169
bipolar 119
classification by form 112
Deiter's (Golgi's Type I) 113, 116
— general structure of 115
Nerve Golgi (Type II) 113
— granular, of cerebellum 115 171
— horizontal, of retina 271
— motor, of anterior horn 161
— multipolar 116
— neuroblasts 110
— neuro-epithelial 119
— neurofibrils 116
— pigment in 116
— polymorphous 118, 164
— principal types of 112
— of Purkinje 117, 169
— pyramidal 117, 163
— size of 112
— small cortical 169
— of spinal ganglia 118, 176
— sympathetic 113, 119
— tract 161
— unipolar 118
Nerve fibers 111, 122
— of cerebellar cortex 171
— of cerebral cortex 167
— climbing 171
— layer of, retinal 270
— medullated 123
— — of cerebellar cortex 171
— — of cerebral cortex 167
— — of peripheral nerves 123, 175
— mossy 171
— non-medullated 127
— tangential 164
Nerve impulse 121
— in retina 274
Nerve terminations, peripheral 177
— end bulbs 181
free 178
motor 177
secretory 178
sensory 178
terminal corpuscles 179
Nerves, peripheral 175
— roots of spinal 182
Nervous system 160
— central 160
— peripheral 174
— systematic 120
Nervous tissue 110
Neumann, sheath of 185
Neurite = axone 112, 122

Neuroblasts 110
Neuro-epithelial cells 119
Neuro-epithelium of maculae acusticae 284
— of olfactory organ 119
— of retina 119, 271
Neurofibrils 5, 9, 116
Neuroglia 110, 128
— cells 128
— of cerebellum 171
— of cerebral cortex 168
— ependymal 128
— fibers 128
— of spinal cord 162
— spongioblasts 110
Neurokeratin 125
Neurolemma 119, 123, 126
Neuromuscular sense-organ 179
Neurone(s) 111
— axone 112
— body of (nerve cell) 111
— centrosomes in 115
— chromatophilic substance 115
— contact and continuity, theories of 111, 121
— dendrites 112
— medullary sheath 124
— — incisures of Schmidt-Lantermann 125
— — nodes of Ranvier 125
— neurofibrils 116
— neurolemma (sheath of Schwann) 126
— neuroplasm 115
— Nissl (tigroid) bodies 115
— pigment in 116
— trophospongium 116
— transference of impulses 121, 122
Neuropil 121
Neutrophilic leucocytes 89
Nipple 310
Nissl bodies 115
Node of Ranvier 124, 125
Nodules, lymphatic, agminated 211
— solitary 211
— of spleen 152
— of tonsils 204
Non-medullated nerve fibers 127
Normoblasts 91
Normocytes 83
Notochord 78, 140
Nuclear division 20
— membrane 9
— network 10
Nuclei of brain 163
Nuclei of Schwann 126
Nucleolus 11
Nucleus 9
— achromatic element (linin) 10
— basi- and oxy-chromatin 11
— dorsalis of spinal cord 161
— of lens 279
— in life of the cell 12
— pulposus 78, 140
— pycnotic 29
Nuel, space of 289
Nuhn, gland of 203
Nutrient canal 133

O.

Occipital lobe of brain 167
Odontoblasts 184, 188, 189
Oesophagus 205
— glands of 205
— vessels and nerves of 206
Oleo-margarin, crystals of 70
Olfactory cells 295
— glands 222
— nerve 123, 295
Oligodendroglia 129, 130
Omentum, great 220
Oöcytes 251
Oögenesis 251
Oögonia 251
Oölemma 141, 250
Optic nerve 277
— papilla 278
Ora serrata 276
Oral cavity 183
— glands of 193
— — vessels and nerves of 200
— — mucous membrane of 183
Orbiculus ciliaris 265
Organ(s) of Corti (organon spirale) 287
— of digestion 182
— enamel 187
— of Giraldes (paradidymis) 247
— of hearing 283
— kinetic, of cell 12, 40
— of muscular system 158
— of nervous system 160
Organ(s) of reproduction, female 249
— — male 237
— of respiration 221
— of skeletal system 131
— of smell 295
— of taste 294
— urinary 229
— of the vascular systems 141
— of vision 261
Osmic acid, demonstration of fat by 70
Ossein 78
Ossification, endochondral 136
— intramembranous 138
— perichondral 137
— post-embryonic 139
Osteoblasts 81, 136, 138
Osteoclasts 81, 136
Osteocytes 79
Otolithic membrane 284
Otoliths 284
Ovary 249
— corpus albicans 253
— — luteum 252
— egg-tubes of Pflüger 250
— follicular atresia 253
— follicles, Graefian 249
— germinal epithelium 249
— haematoidin crystals 253
— lutein cells 252
— oögenesis 251
— ovum 251
— primitive (primordial) follicle 250
— secretion by 252
— tunica albuginea 249
— vessels and nerves of 252
— vestigial structures of 254
Oviduct 254
— vessels and nerves of 255
Ovula Nabothi 256
Ovum 250, 251, 253
— Oögenesis and maturation 251
Oxychromatin 11

P.

Palate, hard 203
— soft 203
Palatine tonsil 204
Pancreas, endocrine portion 219
— exocrine portion 218

Pancreas, islands of Langerhans 219
Panniculus adiposus 299
Paneth, cells of 209
Papilla nervi optici 278
Papillae 35, 201
— circumvallate or vallate 201
conicae (filiformes) 201
of corium 298
dental 187
distinguished from villi 201
of epidermis 298
filiform 201
foliate 202
fungiform 201
of hair 300, 302
of larynx 223
of lip 183
renal 236
of tongue 201
Papillary ducts 236
Paracentral lobule 164, 167
Paradidymis 247
Paraganglia 177
Parametrium 257
Paramitome 3
Paranuclein 12
Paranucleus of cells 5
— of spermatids 241
Paraplasm 5
Parasites of oral cavity 200
Parathyreoid glands 229
Parenchyma of glands 46
Parietal cells 207
— peritoneum 220
— pleura 228
Paroöphoron 254
Parotid gland 196
Pars caeca retinae 276
cartilaginea of Eustachian tube 292
cavernosa urethrae 248
ciliaris retinae 276
convoluta of uriniferous tubule of kidney 230
iridica retinae 276
membranacea urethrae 248
optica retina 269
ossea of Eustachian tube 292
prostatica of urethra 248
radiata of renal cortex 230
recta of kidney 230
Passage, external auditory 293
Pavement epithelium 34
Pearls, epithelial 191
Pellicula 14
Pelvis renalis 235
Pencilli 154
Penis 247
Penchondrium 67, 75, 135
Perimysium 142
— externum 158
— internum 106, 158
Perineurium 175
Periosteum 67, 133, 138
Peritoneum 220
Petit, canal of 280
Peyer's patches 211
Pflüger, egg-tubes of 250
Phaeochrome (chromaffine) cells 121, 177, 260
Phagocytosis 19, 55, 93
— in liver 216
— in lung 226
Pharynx 204
Pharyngeal tonsil 205
Pia mater 173
Pigment 8, 15
— anthracotic in lung 226
— autochthonous 15
in connective tissue 51
in hair 301
in iris 266
iron-holding 17
in nerve cells 116, 119
in skin 298, 299
varieties of 15—17
Pigmentary epithelium of retina 267
Pineal body (epiphysis cerebri) 172
Pituitary body 171
Plasma cells 56
Plasmosomes 4
Plasmodium 14
Plastochondria 4
Plastocontes 4
Plastin 10
Plastosomes 4
Platelets of blood 90
Pleura 228
Plexus chorioidei 173
Plexus gangliosus ciliaris 267
— inter-radiary 168
Plexus myentericus (of Auerbach) 183, 212
— myospermaticus 247
— submucosus (of Meissner) 183, 212
— super-radiary 168
Plica semilunaris 281
Plicae circulares 210
Polar arrangement of chromosomes 21
radiation from centrosomes 24, 25
Polykaryocytes 13, 20, 81
Polymorphous cells of cerebral cortex 118, 164
Pore, taste 294
Portal vein 213
— branches of 214
Precapillary arterioles 143
Precollagenous fibers 60
Precuneus 167
Predentine 189
Pre-elastic fibers 62
Prepuce (praeputium) 247
Prickle cells 296
Primitive (primordial) follicles 250
Prisms of enamel 185
Processes, ciliary 265
Processus vermiformis 211
Prophase 21
Prostate gland 237
Prostatic sinus 238
Protoplasm 2
Proximal convoluted tubule 231
Pseudo-arcades of renal vessels 234
Pseudo-chromosomes 5
Pseudo-nucleoleus 10
Pseudopodia 18
Pseudo-reduction of chromosomes 241
Pulmonary lobule 226
Pulp cavity 184
— enamel 188
— splenic 152, 155
— of tooth 184
Purkinje, cells of 117
— fibers of 110
Pycnosis 29
Pyloric glands 207, 208
Pyramidal cells of cerebral cortex 163

Pyramidal tracts of spinal cord 163
Pyrenin 12

R.

Radiation from centrosome 24
Ranvier, crosses of 126
— node of 125
Rectum 210
Red blood cells (erythrocytes) 82
— in bone marrow 91, 134
— nucleated 85, 86
— in spleen 155
Red marrow 134
— cells of 91
Reduction of chromosomes 241
— division 28, 241
Reflex bundles of spinal cord 161, 162
Reissner's membrane 285
Remak, fibers of 127
Renal corpuscles 230
Reproductive organs
— female 249
— — external genitalia 258
— — ovary 249
— — oviduct (tuba uterina, Fallopian tube) 254
— — uterus 255
— — vagina 257
— — vestigial structures 254
— male 237
— — Cowper's glands 238
— — ductus deferens 245
— — ejaculatory ducts 246
— — epididymis 244
— — penis 247
— — prostate gland 237
— — seminal vesicle 246
— — spermatogenesis 240
— — sperms (spermatozoa) 241
— — testis 238
Respiratory bronchioles 225
— epithelium 225
— system 221
— — bronchi 223, 224
— — larynx 222
— — lungs 224
— — nasal passages 221
— — trachea 223
Rete testis 244
Reticular apparatus of Golgi 5
Reticular relation to secretion 6
— connective tissue 72
— — of liver 216
— fibers 60
— glands 49, 50
Reticulo-endothelium 95
Reticulum 72
— fibers 60
— — of hepatic lobule 216
— — of Müller 268
Retina 267
— pars caeca 276
— — ciliaris 276
— — iridica 276
— — optica 260
— — — fiber-baskets 270, 273
— — — fibers of Müller 269
— — — fovea centralis 275
— — — layers of 269
— — — macula lutea 275
— — — ora serrata 276
— — — rods and cones 274
— — — visual purple 274
— — vessels of 277
Retzius fibers of 289
— lines of 186
Rod ellipsoid 274
— fiber 273
— granule 273
Rods of Corti 287
Rolando, substantia gelatinosa of 161
Root sheath of hair, inner 301
— — — — outer 302
Rouget's cells 147
Ruffini, corpuscles (spindles) of 179

S.

Saliva 200
Salivary corpuscles 200
— ducts 196
— general structure of 193
— glands 196
— special features of 196
Sacrolemma 101, 105
Sarcoplasm 101, 103
Sarcosomes 104
Sarcous discs of Bowman 102
Satellite cells 129
Scala media (cochlear duct) 285
— tympani 286
Scala vestibuli 285
Schlemm, canal of 263
Schmidt, buds of 229
Schmidt-Lantermann, incisures of 125
Schreger, lines of 186
Schwann, cells of 176
— nuclei of 126
— sheath of 119, 123, 126
Scleral swelling 263
Sclerotic coat 261
— cornea 261
— sclera 262
— — vessels and nerves of 263
Sebaceous glands 306
Sebum 306
Secondary constituents of body 31
— dentine 187
— papillae of tongue 261
— nodules (see lymph nodules)
— tendon bundles 160
Secretion 42
— antecedents of 44
— canaliculi 45
— cell nucleus during 46
— varieties of 43
Semen 241
Semicircular canals 283
Seminal ducts 244
— fluid 241, 244
— vesicle 246
Seminiferous tubules 239
— epithelium 239
— spermatogenesis 240
Septula testis 238
Septum penis 247
Septum posterius of spinal cord 163
Serous glands 275
Sertoli, cells of 239
Shadow corpuscles 85
Sharpey's fibers 133, 140, 305
Sheath of Henle (endoneural) 175
— medullary 124
— — nuclei of 126
— of Neumann 185
— of Schwann 123, 126
Shrapnell's membrane 291
Short-rayed astrocytes 129
Silver nitrate, reaction with intercellular cement 30
Sinus, of lymph gland 150

Sinus, prostaticus 238
  splenic 154
— urogenitalis 248
— venosus sclerae 263
Skeletal system 131
Skin 296
  corium (derma) 298
  corpuscles of 300
  epidermis 296
  glands of 306
  hair 300
  nails 305
  papillae of 298
  vessels and nerves of 299
Small intestine 209
Smell, organ of 295
Smooth muscle 96
— nerve terminations of 178
Sole-plate 177
Solitary follicles, of intestine 211
— — of larynx 223
Somite, development of connective tissue from 52
Space of Nuel 289
— — Tenon 263
Spaces of Fontana (spatia anguli iridis) 267
Spangaro, crystals of 238
Spatia zonularia 280
Spermatic cord 246
— fluid 241, 244
Spermatids 240
Spermatoblasts 243
Spermatocytes 240
Spermatogenesis 240, 243
— maturation 241
— wave of 244
Spermatogenia 240
Spermatozoa (sperms) 241
— abnormal 242
— formation of 243
— structure of 242
Sphincter muscle of pupil 266
Spinal cord 160
  anterior funiculus 162, 163
  cells of 161
  central canal 162
  gray matter 161
  lateral funiculus 162, 163
  membranes of 172
  multipolar cells of anterior cornu 161
Spinal posterior funiculus 163
— root fibers, posterior or sensory, course of 162
— substantia gelatinosa of Rolando 161
Spinal ganglia 176
— nerve cells 119
Sphincter urethrae 249
Spirillae 200
Spindle, achromatic 24
— neuromuscular 179
— neurotendinous of Golgi 179
— of Ruffini 179
Spiral ganglion 289, 290
— lamina 285
— membrane of spermatozoa 242
— sulci external and internal 286
Spireme 21
Spleen 151
  accessory spleens 156
  capsule 152
  cells 155
  parenchyma 152
  sinus 154
  vessels and nerves of 152, 156
Splenic corpuscles (of Malpighi) 152
Spongioblasts 110
Spongy (cancellous) bone 131
Spot, Mongolian 299
Stalked hydatid 247
Statoliths 284
Stellate cells of Kupffer 216
— veins (of Verheyn) 234
Stereocilia 39
Stomach 206
— crypts 206
— glands 207
— vessels and nerves of 212
Stomata 220
Straight arteries and veins of kidney 234
— tubules of testis 244
Stratum cinereum 169
  corneum 296
  cylindricum 296
— dentatum 296
  elasticum subcapillare 264
  — supercapillare 264
  gangliosum 168, 169
  germinativum 296
  granulosum of cerebellum 169
Stratum granulosum of skin 296, 298
  lucidum 296, 298
  Malpighi (mucosum) 296
  papillare 298
  pigmenti 267
  proprium iridis 266
  reticulare 298
— spinosum 296
  synoviale 141
  zonale 161
Stria vascularis 286
Striated muscle 99
Striation of muscle fiber 101, 102
Strings (cords, fibers) of Corti 287
Stroma of glands 46
Subarachnoidal space 65
Sublingual gland 198
Sublobular vein in liver 215
Submaxillary gland 197
Substantia lentis 279
Substantia propria corneae 66, 262
Sudoriparous glands 307
Sulcus, external spiral 286
— internal spiral 286
Superior parietal lobule 167
Supporting tissue 52
Super-radiary plexus 168
Suprarenal gland 177, 258
— vessels and nerves of 260
Suspensory ligament of lens 278
Sweat glands 307
Sympathetic nervous system 120
— nerve cells of 119, 120
  ganglia 176
— nerves 175
  plexus of Auerbach 212
  plexus of Meissner 212
Symphysis pubis 73
Synapsis of chromosomes 251
Synarthroses 140
Synchondroses 140
Syncytium 14
Syndesmoses 140
Synovial membrane and villi 140

T.

Tactile cells of Merkel 179, 180
— corpuscles 180
— disc (meniscus) 180
Taenia coli 211
Tangential fibers 164, 168

Tapetum lucidum 264
Tarsal glands 281
— muscle of Riolanus 280
Tarsus of eyelid 73, 281
Taste buds 223, 294
— canal (pore) 294
— cells 294
— hairs 294
— organ of 294
Teeth 184
— auditory of Huschke 286
— cement 184, 186, 193
— dentine 185
— development of 187
— enamel 185
— permanent, development of 193
— pulp 184
— root 191
— vessels and nerves of 187
Tela subcutanea 296, 299
Telae chorioideae 111, 173
Telodendron 111
Telophase 28
Temporal lobe of brain 167
Tendinous tissue 66
Tendon as organ 159
— junction with muscle 160
— sheath 160
— spindle 160, 179
— wing cells 66
Tenon, space of 263
Tensor chorioideae 265
Terminal bars 39
Terminations, peripheral of nerves 177
Territorial organization of cartilage 75
Testis, lobules of 238
— interstitial cells of 238
— tubules of, contorted 239
— — — straight 244
— vessels and nerves of 244
Theca folliculi 250
Thread cells 281
Thrombocytes 90
Thymus gland 156
— involution of 158
— of newborn and adult 157
— vessels and nerves of 158
Thyroid gland 228
Tigroid bodies 115
Tissue, definition of 32
— cavernous (erectile) 247
— lymphatic (adenoid) 72
— varieties of 32
Tomes' fibers 189
— granular layer 185
— process 189
Tongue 200
— lymphatic structures of 202
— papillary and follicular portions 200
— taste buds 202, 294
Tonsil, palatine 204
— pharyngeal 205
Tonofibrils 5, 41, 81, 297, 307
Trabeculae of lymph glands 149
— of spleen 152
Trachea 223
Traction fibers 24
Tracts of spinal cord 162, 163
Tractus centralis of thymus 157
Transformations theory of thymus 156
Transitional epithelium 36, 235
Trichohyalin 42, 301
Trophospongium 6, 116
Trunk fibers of spinal cord 161
Tuba auditiva (Eustachii) 292
— uterina (oviduct) 254
Tubular glands 49
Tubules, contorted (seminiferous) 239
— renal (uriniferous) 230
— — collecting 233
— — convoluted 230, 231, 233
— straight, of testis 244
Tubulo-alveolar glands 49
Tunica adventitia (externa) of arteries 143
— of lymphatic vessels 148
— of veins 147
Tunica albuginea of ovary 249
— — of penis 247
— — of testis 238
— — of spleen 152
— conjunctiva 281
— elastica externa 144
— fibrosa renis 233
— interna (intima) 143
— media 143
— mucosa of digestive tract 182
— — linguae 200
Tunica muscularis of digestive tract 182
— propria of bronchi 225
— — of digestive tract 182
— serosa, of digestive tract 182
— vaginalis, of testis 238
Tunicae albugineae 67
Tunnel of Corti 287
Turgor of nucleus 9
Twin ganglion cells of retina 270
Tympanal investing layer 287
Tympanic cavity 291
— vessels and nerves of 292
Tympanic membrane 290
Tyson, glands of 247

U.

Ureter 253
Urethra, female 236, 248
— male 248
— — corpus cavernosum of 247
Urinary bladder 236
— organs 229
— tract, vessels and nerves of 237
Uriniferous tubules 229
Unipolar nerve cells 118
Uterus 255
— masculinus (sinus prostaticus) 238
— in menstruation 256
— vessels and nerves of 257
Utriculus 283
Uvea 264
Uvula 203

V.

Vacuole, juxtanuclear 56
Vagina 257
Valves of heart 142
— of veins 146
Vas (ductus) deferens 245
— spirale 287
Vasa afferentia and efferentia, of kidney 234
— — of lymph glands 149
— efferentia testis (ductuli efferentes testis) 244
— vasorum 145
Vascular system 141
Vater-Pacinian corpuscles 181

Vein(s) 141, 145
— arcuate (arciform) 234
— bronchial 227
— central, of hepatic lobule 214
— centralis retinae 277
— dorsal, of penis 146
— emissary, of penis 247
— interlobular, of liver 214
— — of kidneys 234
— special features of 152
— splenic 152
— stellate (of Verheyn) 234
— sublobular 215
— valves of 146
Venulae rectae of kidney 234
— stellatae of kidney 234
Verheyn, stellate veins of 234
Vermiform appendix 211
Vertebral artery 144
Vesicula germinativa 251
— seminalis 246
Vestibular glands 258
— membrane 286
Vibrissae 221
Vicq d'Azyr, line of 168
Villi, synovial 140
— of intestine 209
Villus, definition of 201
Vision, organ of 261
Visual purple 274
— cells 271
Vitreous humor 279
Vocal cords 223
Volkmann's canals 132

W.

Wagner, corpuscles of 180
Wandering cells 58
Wax of ear 293
Wharton's jelly 63
Wheel nucleus of plasma cells 56
White (colorless) blood cells 86
— matter of spinal cord 124, 162
— connective-tissue (collagenous) fibers 58
Wing cells of tendon 66
Wolfring, glands of 281

Y.

Yellow bone marrow 134
— connective-tissue (elastic) fibers 59
Yolk granules of egg-cells 8, 251

Z.

Zeiss, glands of 280
Zinn, zonule of 279
Zona fasciculata 259
— glomerulosa 259
— pectinata 289
— pellucida 250
— reticularis 259
— spongiosa 161
— tecta 289
Zonula ciliaris (of Zinn) 279
Zygote 1
Zymogen granules 44
— of pancreas 218

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